

=> d his

(FILE 'HOME' ENTERED AT 15:22:31 ON 02 FEB 2004)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 15:22:50 ON 02 FEB 2004
E ALBUMIN/CT

L1 753 S E3
L2 132 S E11
E E47+ALL
L3 80101 S E2+NT
E E33+ALL
L4 566 S E3,E2
L5 25218 S E2+NT
L6 157881 S ?ALBUMIN?
L7 181833 S L1-L6
L8 2969 S BDNF OR BD NF
L9 2881 S BRAIN DERIVED NEUROTROPHIC FACTOR
L10 2883 S (BD OR BRAIN DERIVED) () (NF OR NEUROTROPHIC FACTOR)
E NEUROTROPHIC FACTOR/CT
L11 141 S E10
L12 2554 S E26
E E25+ALL
L13 789 S E3-E5 AND BRAIN DERIVED
L14 679 S E12,E13
L15 3242 S E2+NT (L) BRAIN DERIVED
L16 64 S L7 AND L8-L15
L17 19234 S INTERFERONALPHA OR ALPHainterferon OR INTERFERONBETA OR BETAI
E INTERFERON/CT
L18 302 S E3-E19
L19 18390 S E85-E101
E INTERFERONS/CT
E E3+ALL
L20 18391 S E7,E6 (L) (ALPHA OR BETA)
L21 546 S L7 AND L17-L20
L22 2340 S TIMP() (I OR 1)

FILE 'REGISTRY' ENTERED AT 15:29:36 ON 02 FEB 2004
L23 1 S 140208-24-8

FILE 'HCAPLUS' ENTERED AT 15:30:37 ON 02 FEB 2004

L24 2026 S L23
L25 859 S TISSUE INHIBITOR(1W)METALLOPROTEINASE 1
L26 27 S METALLOPROTEINASE INHIBITOR 1
L27 651 S TIMP1
L28 12 S FIBROBLAST COLLAGENASE INHIBITOR
L29 91 S L7 AND L22,L24-L28
L30 678 S L16,L21,L29
L31 9815 S IFNALPHA OR IFNBETA OR ALPHAIFN OR BETAIFN OR IFN(A) (ALPHA OR
L32 119 S L7 AND L31
L33 700 S L30,L32
L34 62 S L33 AND (FUSION OR FUSE OR FUSED OR FUSES OR FUSING)
L35 167 S L33 AND RECOMBIN?
L36 44 S L33 AND CHIMER?
L37 202 S L34-L36
E ROSEN C/AU
L38 27 S E3,E4
E ROSEN CRAIG/AU
L39 625 S E3-E5
E HASELTINE W/AU
L40 302 S E3,E4,E7-E10
L41 10 S L33 AND L38-L40
E HUMAN GENOME SCI/PA,CS

L42	975 S E5-E37
L43	13 S L33 AND L42
L44	13 S L41,L43
L45	13 S L44 AND L37
L46	9 S L45 AND (SHELF LIFE OR SHELF LIFE)
L47	4 S L45 NOT L46
	SEL DN AN 1 4
L48	2 S L47 NOT E1-E6
L49	11 S L46,L48
	SEL RN
	DEL SEL
	E FUSION PROTEIN/CT
L50	11933 S E9
	E E9+ALL
L51	3795 S E3,E4
L52	5 S L51 AND L33
L53	29 S L50 AND L33
L54	34 S L49,L52,L53
L55	27 S L54 AND ALBUMIN
L56	7 S L54 NOT L55
L57	159 S L37 AND ALBUMIN
L58	132 S L57 NOT L43-L49,L52-L56
L59	6 S L58 AND L16
L60	7 S L58 AND L29
L61	121 S L58 NOT L59,L60
L62	96 S L61 AND (PD<=20000412 OR PRD<=20000412 OR AD<=20000412) SEL DN AN 9 12 13 24 29 31 35 39 44 47 55 58 72 74 83 85 92 93
L63	18 S L62 AND E1-E54
L64	29 S L49,L63 AND L1-L22,L24-L63
L65	29 S L64 AND ?ALBUMIN?
L66	29 S L64 AND (INF? OR INTERFERON OR TIMP? OR NEUROTROPHIC?)

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 16:00:16 ON 02 FEB 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 2 Feb 2004 VOL 140 ISS 6
FILE LAST UPDATED: 1 Feb 2004 (20040201/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot

L66	ANSWER 1 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN	2003:571103 HCAPLUS
DN	139:122690
ED	Entered STN: 25 Jul 2003
TI	Albumin fusion proteins for prolonged shelf-life of therapeutic proteins

IN Ballance, David James; Turner, Andrew John; Rosen, Craig A.; Haseltine, William A.

PA Human Genome Sciences, Inc., USA; Delta Biotechnology Limited; Principia Pharmaceutical Corporation

SO PCT Int. Appl., 598 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C12N

CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 3

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003060071	A2	20030724	WO 2002-US40891	20021223
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 2001-341811P	P	20011221		
	US 2002-350358P	P	20020124		
	US 2002-351360P	P	20020128		
	US 2002-359370P	P	20020226		
	US 2002-360000P	P	20020228		
	US 2002-367500P	P	20020327		
	US 2002-370227P	P	20020408		
	US 2002-378950P	P	20020510		
	US 2002-382617P	P	20020524		
	US 2002-383123P	P	20020528		
	US 2002-385708P	P	20020605		
	US 2002-394625P	P	20020710		
	US 2002-398008P	P	20020724		
	US 2002-402131P	P	20020809		
	US 2002-402708P	P	20020813		
	US 2002-411355P	P	20020918		
	US 2002-411426P	P	20020918		
	US 2002-414984P	P	20021002		
	US 2002-417611P	P	20021011		
	US 2002-420246P	P	20021023		
	US 2002-423623P	P	20021105		

AB The present invention encompasses albumin fusion proteins. Many therapeutic proteins in their native state or when recombinantly produced are typically labile mols. exhibiting short shelf-lives, particularly when formulated in aqueous solns.; fusions of the therapeutic protein with human serum albumin have a longer serum half-life and/or stabilized activity in solution (or in a pharmaceutical composition) in vitro and/or in vivo than the corresponding unfused therapeutic mols. Thus, albumin fusion proteins are provided comprising granulocyte colony-stimulating factor, interleukin 2, parathormone, erythropoietin, interferon β , interferon α_2 , interferon A/D hybrid, a single-chain insulin analog, growth hormone, and (7-36)GLP-1. Nucleic acid mols. encoding the albumin fusion proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the albumin fusion proteins of the invention and using these nucleic acids, vectors, and/or host cells. Addnl. the present invention encompasses pharmaceutical compns. comprising albumin fusion proteins and methods of treating or preventing diseases,

disorders or conditions related to diabetes mellitus using albumin fusion proteins of the invention.

ST albumin fusion therapeutic protein shelflife

IT Animal cell line
(293, recombinant expression host; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Animal cell line
(CHO, recombinant expression host; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Animal cell line
(NSO, recombinant expression host; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiviral, T1249 peptide inhibitor derived from HIV-1; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Antidiabetic agents
Human
Linking agents
Molecular cloning
(human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Fusion proteins (chimeric proteins)
Interleukin 2
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Signal peptides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Animal cell
(mammalian, recombinant expression host; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Diabetes mellitus
(non-insulin-dependent, treatment of; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Protein sequences
(of human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Plasmid vectors
(pC4; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Plasmid vectors
(pEE12.1; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Plasmid vectors
(pSAC35; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Saccharomyces cerevisiae
Yeast
(recombinant expression host that is glycosylation and protease-deficient; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Albumins, biological studies
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(serum; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Interferons
 RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (α2; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Interferons
 RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (α; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Interferons
 RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (αD; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Interferons
 RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (β; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT 562119-52-2P 562119-53-3P 562119-54-4P 562119-55-5P 562119-56-6P
 562119-57-7P 562119-58-8P 562119-59-9P 562119-60-2P 562119-61-3P
 562119-62-4P 562119-63-5P 562119-64-6P 562119-65-7P 562119-66-8P
 562119-67-9P 562119-68-0P 562119-69-1P 562119-70-4P 562119-71-5P
 562119-72-6P 562119-73-7P 562119-74-8P 562119-75-9P 562119-76-0P
 562119-77-1P 562119-78-2P 562119-79-3P 562119-80-6P 562119-81-7P
 562119-82-8P 562119-83-9P 562119-85-1DP, Albumin (human),
 subfragments, fusion products
 RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (amino acid sequence; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT 9002-64-6P, Parathormone 9004-10-8P, Insulin, biological studies
 11096-26-7P, Erythropoietin 89750-14-1P, Glucagon-like peptide I
 143011-72-7P, Granulocyte colony-stimulating factor
 RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT 562119-84-0
 RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
 (nucleotide sequence; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT 562125-97-7 562125-98-8 562125-99-9 562126-00-5 562126-01-6
 562126-02-7 562126-03-8 562126-04-9 562126-05-0 562126-06-1
 562126-07-2 562126-08-3 562126-09-4 562126-10-7 562126-11-8
 562126-12-9 562126-13-0 562126-14-1 562126-15-2 562126-16-3
 562126-17-4 562126-18-5 562126-19-6 562126-20-9 562126-21-0
 562126-22-1 562126-23-2 562126-24-3 562126-25-4 562126-26-5
 562126-27-6 562126-28-7 562126-29-8 562126-30-1 562126-31-2
 562126-32-3 562126-33-4 562126-34-5 562126-35-6 562126-36-7
 562126-37-8 562126-38-9 562126-39-0 562126-40-3 562126-41-4
 562126-42-5 562126-43-6 562126-44-7 562126-45-8 562126-46-9
 562126-47-0 562126-48-1 562126-49-2 562126-50-5 562126-51-6

562126-52-7	562126-53-8	562126-54-9	562126-55-0	562126-56-1
562126-57-2	562126-58-3	562126-59-4	562126-60-7	562126-61-8
562126-62-9	562126-63-0	562126-64-1	562126-65-2	562126-66-3
562126-67-4	562126-68-5	562126-69-6	562126-70-9	562126-71-0
562126-72-1	562126-73-2	562126-74-3	562126-75-4	562126-76-5
562126-77-6	562126-78-7	562126-79-8	562126-80-1	562126-81-2
562126-82-3	562126-83-4	562126-84-5	562126-85-6	562126-86-7
562128-87-4	562128-88-5	562128-89-6	562128-90-9	562128-91-0
562128-92-1	562128-93-2	562128-94-3	562128-95-4	562128-96-5
562128-97-6	562128-98-7	562128-99-8	562129-00-4	562129-01-5
562129-02-6	562129-03-7	562129-04-8	562129-05-9	562129-06-0
562129-07-1	562129-08-2	562129-09-3	562129-10-6	562129-11-7
562129-12-8	562129-13-9	562129-14-0	562129-15-1	562129-16-2
562129-17-3	562129-18-4	562129-19-5	562129-20-8	562129-21-9
562129-22-0	562129-23-1	562129-24-2	562129-25-3	562129-26-4
562129-27-5	562129-28-6	562129-29-7	562129-30-0	562129-31-1
562129-32-2	562129-33-3	562129-34-4	562129-35-5	562129-36-6
562129-37-7	562129-38-8	562129-39-9	562129-40-2	562129-41-3
562129-42-4	562129-43-5	562129-44-6	562129-45-7	562129-46-8
562129-47-9	562129-48-0	562129-49-1	562129-50-4	562129-51-5
562129-52-6	562129-53-7	562129-54-8	562129-55-9	562129-56-0
562129-57-1	562129-58-2	562129-59-3	562129-60-6	562129-61-7
562129-62-8	562129-63-9	562129-64-0	562129-65-1	562129-66-2
562129-67-3	562129-68-4	562129-69-5	562129-70-8	562129-71-9
562129-72-0	562129-73-1	562129-74-2	562129-75-3	562129-76-4
562129-77-5	562129-78-6	562129-79-7	562129-80-0	562129-81-1
562129-82-2	562129-83-3	562129-84-4	562129-85-5	562129-86-6
562129-87-7	562129-88-8	562129-89-9	562129-90-2	562129-91-3
562129-92-4	562129-93-5	562129-94-6	562129-95-7	562129-96-8
562129-97-9	562129-98-0	562129-99-1	562130-00-1	562130-01-2
562130-02-3	562130-03-4	562130-04-5	562130-05-6	562130-06-7
562130-07-8	562130-08-9	562130-09-0	562130-10-3	562130-11-4
562130-12-5	562130-13-6	562130-14-7	562130-15-8	562130-16-9
562130-17-0	562130-18-1	562130-19-2	562130-20-5	562130-21-6
562130-22-7	562130-23-8	562130-24-9	562130-25-0	562130-26-1
562130-27-2	562130-28-3	562130-29-4	562130-30-7	562130-31-8
562130-32-9	562130-33-0	562130-34-1	562130-35-2	562130-36-3

RL: PRP (Properties)

(unclaimed nucleotide sequence; albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT	562130-37-4	562130-38-5	562130-39-6	562130-40-9	562130-41-0
	562130-42-1	562130-43-2	562130-44-3	562130-45-4	562130-46-5
	562130-47-6	562130-48-7	562130-49-8	562130-50-1	562130-51-2
	562130-52-3	562130-53-4	562130-54-5	562130-55-6	562130-56-7
	562130-57-8	562130-58-9	562130-59-0	562130-60-3	562130-61-4
	562130-62-5	562130-63-6	562130-64-7	562130-65-8	562130-66-9
	562130-67-0	562130-68-1	562130-69-2	562130-70-5	562130-71-6
	562130-72-7	562130-73-8	562130-74-9	562130-75-0	562130-76-1
	562130-77-2	562130-78-3	562130-79-4	562130-80-7	562130-81-8
	562130-82-9	562130-83-0	562130-84-1	562130-85-2	562130-86-3
	562130-87-4	562130-88-5	562130-89-6	562130-90-9	562130-91-0
	562130-92-1	562130-93-2	562130-94-3	562130-95-4	562130-96-5
	562130-97-6	562130-98-7	562130-99-8	562131-00-4	562131-01-5
	562131-02-6	562131-03-7	562131-04-8	562131-05-9	562131-06-0
	562131-07-1	562131-08-2	562131-09-3	562131-10-6	562131-11-7
	562131-12-8	562131-13-9	562131-14-0	562131-15-1	562131-16-2
	562131-17-3	562131-18-4	562131-19-5	562131-20-8	562131-21-9
	562131-22-0	562131-23-1	562131-24-2	562131-25-3	562131-26-4
	562131-27-5	562131-28-6	562131-29-7	562131-30-0	562131-31-1
	562131-32-2	562131-33-3	562131-34-4	562131-35-5	562131-36-6
	562131-37-7	562131-38-8	562131-39-9	562131-40-2	562131-41-3
	562131-42-4	562131-43-5	562131-44-6	562131-45-7	562131-46-8
	562131-47-9	562131-48-0	562131-49-1	562131-50-4	562131-51-5

562131-52-6	562131-53-7	562131-54-8	562131-55-9	562131-56-0
562131-57-1	562131-58-2	562131-59-3	562131-60-6	562131-61-7
562131-62-8	562131-63-9	562131-64-0	562131-65-1	562131-66-2
562131-67-3	562131-68-4	562131-69-5	562131-70-8	562131-71-9
562131-72-0	562131-73-1	562131-74-2	562131-75-3	562131-76-4
562131-77-5	562131-78-6	562131-79-7	562131-80-0	562131-81-1
562131-82-2	562131-83-3	562131-84-4	562131-85-5	562131-86-6
562131-87-7	562131-88-8	562131-89-9	562131-90-2	562131-91-3
562131-92-4	562131-93-5	562131-94-6	562131-95-7	562131-96-8
562131-97-9	562131-98-0	562131-99-1	562132-00-7	562132-01-8
562132-02-9	562132-03-0	562132-04-1	562132-05-2	562132-06-3
562132-07-4	562132-08-5	562132-09-6	562132-10-9	562132-11-0
562132-12-1	562132-13-2	562132-14-3	562132-15-4	562132-16-5
562132-17-6	562132-18-7	562132-19-8	562132-20-1	562132-21-2
562132-22-3	562132-23-4	562132-24-5	562132-25-6	562132-26-7
562132-27-8	562132-28-9	562132-29-0	562132-30-3	562132-32-5
562132-34-7	562132-36-9	562132-37-0	562132-39-2	562132-40-5
562132-41-6	562132-42-7	562132-43-8	562132-44-9	562132-45-0
562132-46-1	562132-47-2	562132-48-3	562132-49-4	562132-50-7
562132-51-8	562132-52-9	562132-53-0	562132-54-1	562132-56-3
562132-58-5	562132-60-9	562132-62-1	562132-64-3	562132-66-5
562132-68-7	562132-70-1	562132-72-3	562132-74-5	562132-76-7
562132-78-9	562132-80-3	562132-82-5	562132-85-8	562132-87-0
562132-89-2	562132-90-5	562132-91-6	562132-92-7	562132-93-8
562132-94-9	562132-95-0	562132-96-1	562132-98-3	562133-00-0

RL: PRP (Properties)

(unclaimed nucleotide sequence; albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT	562133-02-2	562133-03-3	562133-04-4	562133-05-5	562133-06-6
	562133-07-7	562133-08-8	562133-09-9	562133-21-5	562133-22-6
	562133-23-7	562133-24-8	562133-25-9	562133-26-0	562133-27-1
	562133-28-2	562133-29-3	562133-30-6	562133-31-7	562133-33-9
	562133-35-1	562133-36-2	562133-37-3	562133-39-5	562133-40-8
	562133-42-0	562133-44-2	562133-45-3	562133-47-5	562133-49-7
	562133-50-0	562133-53-3	562133-56-6	562133-58-8	562133-59-9
	562133-61-3	562133-63-5	562133-66-8	562133-69-1	562133-70-4
	562133-72-6	562133-74-8	562133-75-9	562133-76-0	562133-77-1
	562133-78-2	562133-79-3	562133-80-6	562133-81-7	562133-82-8
	562133-83-9	562133-84-0	562133-85-1	562133-86-2	562133-87-3
	562133-88-4	562133-89-5	562133-90-8	562133-91-9	562133-92-0
	562133-93-1	562133-94-2	562133-95-3	562133-96-4	562133-97-5
	562133-98-6	562133-99-7	562134-00-3	562134-01-4	562134-02-5
	562134-03-6	562134-04-7	562134-05-8	562134-06-9	562134-07-0
	562134-08-1	562134-09-2	562134-10-5	562134-11-6	562134-12-7
	562134-13-8	562134-14-9	562134-15-0	562134-16-1	562134-17-2
	562134-18-3	562134-19-4	562134-20-7	562134-21-8	562134-22-9
	562134-23-0	562134-24-1	562134-25-2	562134-26-3	562134-27-4
	562134-28-5	562134-29-6	562134-30-9	562134-31-0	562134-32-1
	562136-11-2	562136-12-3	562136-13-4	562136-14-5	562136-15-6
	562136-16-7	562136-17-8	562136-18-9	562136-19-0	562136-20-3
	562136-21-4	562136-22-5	562136-23-6	562136-24-7	562136-25-8
	562136-26-9	562136-27-0	562136-28-1	562136-29-2	562136-30-5
	562136-31-6	562136-32-7	562136-33-8	562136-34-9	562136-35-0
	562136-36-1	562136-37-2	562136-38-3	562136-39-4	562136-40-7
	562136-41-8	562136-42-9	562136-43-0	562136-44-1	562136-45-2
	562136-46-3	562136-47-4	562136-48-5	562136-49-6	562136-50-9
	562136-51-0	562136-52-1	562136-53-2	562136-54-3	562136-55-4
	562136-56-5	562136-57-6	562136-58-7	562136-59-8	562136-60-1
	562136-61-2	562136-62-3	562136-63-4	562136-64-5	562136-65-6
	562136-66-7	562136-67-8	562136-68-9	562136-69-0	562136-70-3
	562136-71-4	562136-72-5	562136-73-6	562136-74-7	562136-75-8
	562136-76-9	562136-77-0	562136-78-1	562136-79-2	562136-80-5
	562136-81-6	562136-82-7	562136-83-8	562136-84-9	562136-85-0

562136-86-1	562136-87-2	562136-88-3	562136-89-4	562136-90-7
562136-91-8	562136-92-9	562136-93-0	562136-94-1	562136-95-2
562136-96-3	562136-97-4	562136-98-5	562136-99-6	562137-00-2
562137-01-3	562137-02-4	562137-03-5	562137-04-6	562137-05-7
562137-06-8	562137-07-9	562137-08-0	562137-09-1	562137-10-4
562137-11-5	562137-12-6	562137-13-7	562137-14-8	562137-15-9
562137-16-0	562137-17-1	562137-18-2	562137-19-3	562137-20-6
562137-21-7	562137-22-8	562137-23-9	562137-24-0	562137-25-1
562137-26-2	562137-27-3	562137-28-4	562137-29-5	562137-30-8
562137-31-9	562137-32-0	562137-33-1	562137-34-2	562137-35-3
562137-36-4	562137-37-5	562137-38-6	562137-39-7	562137-40-0
562137-41-1	562137-42-2	562137-43-3	562137-44-4	562137-45-5
562137-46-6	562137-47-7	562137-48-8	562137-49-9	562137-50-2

RL: PRP (Properties)

(unclaimed nucleotide sequence; albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT	562137-51-3	562137-52-4	562137-53-5	562137-54-6	562137-55-7
	562137-56-8	562137-57-9	562137-58-0	562137-59-1	562137-60-4
	562137-61-5	562137-62-6	562137-63-7	562137-64-8	562137-65-9
	562137-66-0	562137-67-1	562137-68-2	562137-69-3	562137-70-6
	562137-71-7	562137-72-8	562137-73-9	562137-74-0	562137-75-1
	562137-76-2	562137-77-3	562137-78-4	562137-79-5	562137-84-2
	562137-85-3	562137-86-4	562137-87-5	562137-88-6	562137-97-7
	562137-98-8	562137-99-9	562138-00-5	562138-01-6	562138-02-7
	562138-03-8	562138-04-9			

RL: PRP (Properties)

(unclaimed nucleotide sequence; albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT	562126-87-8	562126-88-9	562126-89-0	562126-90-3	562126-91-4
	562126-92-5	562126-93-6	562126-94-7	562126-95-8	562126-96-9
	562126-97-0	562126-98-1	562126-99-2	562127-00-8	562127-01-9
	562127-02-0	562127-03-1	562127-04-2	562127-05-3	562127-06-4
	562127-07-5	562127-08-6	562127-09-7	562127-10-0	562127-11-1
	562127-12-2	562127-13-3	562127-14-4	562127-15-5	562127-16-6
	562127-17-7	562127-18-8	562127-19-9	562127-20-2	562127-21-3
	562127-22-4	562127-23-5	562127-24-6	562127-25-7	562127-26-8
	562127-27-9	562127-28-0	562127-29-1	562127-30-4	562127-31-5
	562127-32-6	562127-33-7	562127-34-8	562127-35-9	562127-36-0
	562127-37-1	562127-38-2	562127-39-3	562127-40-6	562127-41-7
	562127-42-8	562127-43-9	562127-44-0	562127-45-1	562127-46-2
	562127-47-3	562127-48-4	562127-49-5	562127-50-8	562127-51-9
	562127-52-0	562127-53-1	562127-54-2	562127-55-3	562127-56-4
	562127-57-5	562127-58-6	562127-59-7	562127-60-0	562127-61-1
	562127-62-2	562127-63-3	562127-64-4	562127-65-5	562127-66-6
	562127-67-7	562127-68-8	562127-69-9	562127-70-2	562127-71-3
	562127-72-4	562127-73-5	562127-74-6	562127-75-7	562127-76-8
	562127-77-9	562127-78-0	562127-79-1	562127-80-4	562127-81-5
	562127-82-6	562127-83-7	562127-84-8	562127-85-9	562127-86-0
	562127-87-1	562127-88-2	562127-89-3	562127-90-6	562127-91-7
	562127-92-8	562127-93-9	562127-94-0	562127-95-1	562127-96-2
	562127-97-3	562127-98-4	562127-99-5	562128-00-1	562128-01-2
	562128-02-3	562128-03-4	562128-04-5	562128-05-6	562128-06-7
	562128-07-8	562128-08-9	562128-09-0	562128-10-3	562128-11-4
	562128-12-5	562128-13-6	562128-14-7	562128-15-8	562128-16-9
	562128-17-0	562128-18-1	562128-19-2	562128-20-5	562128-21-6
	562128-22-7	562128-23-8	562128-24-9	562128-25-0	562128-26-1
	562128-27-2	562128-28-3	562128-29-4	562128-30-7	562128-31-8
	562128-32-9	562128-33-0	562128-34-1	562128-35-2	562128-36-3
	562128-37-4	562128-38-5	562128-39-6	562128-40-9	562128-41-0
	562128-42-1	562128-43-2	562128-44-3	562128-45-4	562128-46-5
	562128-47-6	562128-48-7	562128-49-8	562128-50-1	562128-51-2
	562128-52-3	562128-53-4	562128-54-5	562128-55-6	562128-56-7
	562128-57-8	562128-58-9	562128-59-0	562128-60-3	562128-61-4

562128-62-5	562128-63-6	562128-64-7	562128-65-8	562128-66-9
562128-67-0	562128-68-1	562128-69-2	562128-70-5	562128-71-6
562128-72-7	562128-73-8	562128-74-9	562128-75-0	562128-76-1
562128-77-2	562128-78-3	562128-79-4	562128-80-7	562128-81-8
562128-82-9	562128-83-0	562128-84-1	562128-85-2	562128-86-3
562132-31-4	562132-33-6	562132-35-8	562132-55-2	562132-57-4
562132-59-6	562132-61-0	562132-63-2	562132-65-4	562132-67-6
562132-69-8	562132-71-2	562132-73-4	562132-75-6	562132-77-8
562132-79-0	562132-81-4	562132-83-6	562132-84-7	562132-86-9
562132-88-1	562132-97-2	562132-99-4	562133-01-1	562133-10-2
562133-11-3	562133-12-4	562133-13-5	562133-14-6	562133-15-7
562133-16-8	562133-17-9	562133-18-0	562133-19-1	562133-20-4
562133-32-8	562133-34-0	562133-38-4	562133-41-9	562133-43-1

RL: PRP (Properties)

(unclaimed protein sequence; albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT	562133-46-4	562133-48-6	562133-51-1	562133-52-2	562133-54-4
	562133-55-5	562133-57-7	562133-60-2	562133-62-4	562133-64-6
	562133-65-7	562133-67-9	562133-68-0	562133-71-5	562133-73-7
	562134-33-2	562134-34-3	562134-35-4	562134-36-5	562134-37-6
	562134-38-7	562134-39-8	562134-40-1	562134-41-2	562134-42-3
	562134-43-4	562134-44-5	562134-45-6	562134-46-7	562134-47-8
	562134-48-9	562134-49-0	562134-50-3	562134-51-4	562134-52-5
	562134-53-6	562134-54-7	562134-55-8	562134-56-9	562134-57-0
	562134-58-1	562134-59-2	562134-60-5	562134-61-6	562134-62-7
	562134-63-8	562134-64-9	562134-65-0	562134-66-1	562134-67-2
	562134-68-3	562134-69-4	562134-70-7	562134-71-8	562134-72-9
	562134-73-0	562134-74-1	562134-75-2	562134-76-3	562134-77-4
	562134-78-5	562134-79-6	562134-80-9	562134-81-0	562134-82-1
	562134-83-2	562134-84-3	562134-85-4	562134-86-5	562134-87-6
	562134-88-7	562134-89-8	562134-90-1	562134-91-2	562134-92-3
	562134-93-4	562134-94-5	562134-95-6	562134-96-7	562134-97-8
	562134-98-9	562134-99-0	562135-00-6	562135-01-7	562135-02-8
	562135-03-9	562135-04-0	562135-05-1	562135-06-2	562135-07-3
	562135-08-4	562135-09-5	562135-10-8	562135-11-9	562135-12-0
	562135-13-1	562135-14-2	562135-15-3	562135-16-4	562135-17-5
	562135-18-6	562135-19-7	562135-20-0	562135-21-1	562135-22-2
	562135-23-3	562135-24-4	562135-25-5	562135-26-6	562135-27-7
	562135-28-8	562135-29-9	562135-30-2	562135-31-3	562135-32-4
	562135-33-5	562135-34-6	562135-35-7	562135-36-8	562135-37-9
	562135-38-0	562135-39-1	562135-40-4	562135-41-5	562135-42-6
	562135-43-7	562135-44-8	562135-45-9	562135-46-0	562135-47-1
	562135-48-2	562135-49-3	562135-50-6	562135-51-7	562135-52-8
	562135-53-9	562135-54-0	562135-55-1	562135-56-2	562135-57-3
	562135-58-4	562135-59-5	562135-60-8	562135-61-9	562135-62-0
	562135-63-1	562135-64-2	562135-65-3	562135-66-4	562135-67-5
	562135-68-6	562135-69-7	562135-70-0	562135-71-1	562135-72-2
	562135-73-3	562135-74-4	562135-75-5	562135-76-6	562135-77-7
	562135-78-8	562135-79-9	562135-80-2	562135-81-3	562135-82-4
	562135-83-5	562135-84-6	562135-85-7	562135-86-8	562135-87-9
	562135-88-0	562135-89-1	562135-90-4	562135-91-5	562135-92-6
	562135-93-7	562135-94-8	562135-95-9	562135-96-0	562135-97-1
	562135-98-2	562135-99-3	562136-00-9	562136-01-0	562136-02-1
	562136-03-2	562136-04-3	562136-05-4	562136-06-5	562136-07-6
	562136-08-7	562136-09-8	562136-10-1	562137-80-8	562137-81-9
	562137-82-0	562137-83-1	562137-89-7	562137-90-0	562137-91-1
	562137-92-2	562137-93-3	562137-94-4	562137-95-5	562137-96-6
	562138-05-0	562138-06-1	562138-07-2	562138-08-3	562138-09-4
	562138-10-7	562138-11-8	562138-12-9	562138-13-0	562138-14-1
	562138-15-2	562138-16-3	562138-17-4		

RL: PRP (Properties)

(unclaimed protein sequence; albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT 2543-43-3 16941-32-5, Glucagon (swine) 16960-16-0,
 α1-24-Corticotropin 33017-11-7, Proinsulin C-peptide (human)
 40958-31-4, Somatostatin (sheep reduced) 62087-72-3 65505-61-5
 75306-06-8, Somatostatin-28 (sheep reduced) 82177-09-1 85482-68-4
 85734-71-0 91917-63-4, Atrial natriuretic peptide-28 (human reduced)
 110543-54-9 118934-21-7 119777-39-8 122024-47-9 125677-89-6
 130912-02-6 131748-18-0 131748-19-1 134374-28-0 147613-04-5
 155709-76-5 166980-40-1 170098-75-6 177339-71-8 192503-43-8
 197520-45-9 247166-37-6 263906-58-7 283148-45-8 313951-59-6
 367273-46-9 367273-47-0 367273-48-1 404935-01-9 477953-25-6
 477953-26-7 477953-27-8 477953-28-9 477953-29-0 477953-30-3
 477953-31-4 477953-32-5 477953-33-6 477953-34-7 477953-35-8
 478188-11-3 478188-13-5 561304-79-8 561304-80-1 561304-81-2
 561304-86-7 561304-88-9 561304-92-5 562077-29-6 562077-30-9
 562077-31-0 562077-32-1 562077-33-2 562077-34-3 562077-35-4
 562077-36-5 562077-37-6 562077-38-7 562077-39-8 562077-40-1
 562077-41-2

RL: PRP (Properties)

(unclaimed sequence; albumin fusion proteins for prolonged shelf-life
 of therapeutic proteins)

L66 ANSWER 2 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:571004 HCAPLUS

DN 139:122689

ED Entered STN: 25 Jul 2003

TI **Albumin fusion proteins for prolonged shelf-life of therapeutic proteins**

IN Rosen, Craig A.; Haseltine, William A.

PA Human Genome Sciences, Inc., USA

SO PCT Int. Appl., 1086 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07K

CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 3

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003059934	A2	20030724	WO 2002-US40892	20021223
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 2001-341811P	P	20011221		
	US 2002-350358P	P	20020124		
	US 2002-359370P	P	20020226		
	US 2002-360000P	P	20020228		
	US 2002-367500P	P	20020327		
	US 2002-370227P	P	20020408		
	US 2002-378950P	P	20020510		
	US 2002-398008P	P	20020724		
	US 2002-402131P	P	20020809		
	US 2002-402708P	P	20020813		
	US 2002-411355P	P	20020918		
	US 2002-414984P	P	20021002		
	US 2002-417611P	P	20021011		

US 2002-420246P P 20021023
 US 2002-423623P P 20021105

- AB The present invention encompasses **albumin fusion** proteins. Many therapeutic proteins in their native state or when recombinantly produced are typically labile mols. exhibiting short shelf-lives, particularly when formulated in aqueous solns.; fusions of the therapeutic protein with human serum albumin have a longer serum half-life and/or stabilized activity in solution (or in a pharmaceutical composition) in vitro and/or in vivo than the corresponding unfused therapeutic mols. Thus, **albumin fusion** proteins are provided comprising **interferon**, **beta**., **interferon** α 2, insulin, bone morphogenetic protein 9, glucagon-like peptide-I(7-36), a hybrid **interferon** A/D, and extendin 4. Nucleic acid mols. encoding the **albumin fusion** proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the **albumin fusion** proteins of the invention and using these nucleic acids, vectors, and/or host cells. Addnl. the present invention encompasses pharmaceutical compns. comprising **albumin fusion** proteins and methods of treating or preventing diseases, disorders or conditions related to diabetes mellitus using **albumin fusion** proteins of the invention.
- ST **albumin fusion therapeutic protein shelflife**
- IT Animal cell line (293, **recombinant** expression host; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT Animal cell line (CHO, **recombinant** expression host; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT Animal cell line (NSO, **recombinant** expression host; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT Metabolism, animal (disorder, treatment of; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT Antidiabetic agents
- IT Antiobesity agents
- IT Cardiovascular agents
- IT Human
- IT Linking agents
- IT Molecular cloning (human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT **Fusion proteins (chimeric proteins)**
 RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT Signal peptides
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT Diabetes mellitus (insulin-dependent, treatment of; human serum **albumin fusion** proteins for prolonged **shelf-life** of

- therapeutic proteins)
- IT Animal cell
(mammalian, **recombinant** expression host; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT Nerve, disease
(neuropathy, treatment of; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT Diabetes mellitus
(non-insulin-dependent, treatment of; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT Protein sequences
(of human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT Plasmid vectors
(pC4; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT Plasmid vectors
(pEE12.1; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT Plasmid vectors
(pSAC35; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT Saccharomyces cerevisiae
Yeast
(**recombinant** expression host that is glycosylation and protease-deficient; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT Eye, disease
(retinopathy, treatment of; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT **Albumins, biological studies**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(serum; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT Cardiovascular system, disease
Endocrine system, disease
Heart, disease
Hyperglycemia
Kidney, disease
Nervous system, disease
Obesity
(treatment of; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT **Interferons**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(α 2; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT **Interferons**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(α ; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic

- IT proteins)
Interferons
 RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (α AD; human serum **albumin**
 fusion proteins for prolonged **shelf-life** of therapeutic proteins)
- IT **Interferons**
 RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (β ; human serum **albumin fusion**
 proteins for prolonged **shelf-life** of therapeutic proteins)
- IT 75306-06-8, Somatostatin-28 (sheep reduced) 561304-81-2 561353-88-6
 RL: PRP (Properties)
 (Unclaimed; **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT 561347-54-4DP, **Albumin** (human), subfragments, **fusion**
 proteins 561347-55-5P 561347-56-6P 561347-57-7P 561347-58-8P
 561347-59-9P 561347-60-2P 561347-61-3P 561347-62-4P 561347-63-5P
 561347-64-6P 561347-65-7P 561347-66-8P 561347-67-9P 561347-68-0P
 561347-69-1P 561347-70-4P 561347-71-5P 561347-72-6P 561347-73-7P
 561347-74-8P 561347-75-9P 561347-76-0P 561347-77-1P 561347-78-2P
 561347-79-3P
 RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (amino acid sequence; human serum **albumin fusion**
 proteins for prolonged **shelf-life** of therapeutic proteins)
- IT 9004-10-8P, Insulin, biological studies 107444-51-9P,
 (7-36)Glucagon-like peptide 1 amide 141732-76-5P, Extendin 4
 305835-60-3P, Bone morphogenetic protein 9
 RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)
- IT 50-99-7, D-Glucose, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (maintenance of basal level of; human serum **albumin**
 fusion proteins for prolonged **shelf-life** of therapeutic proteins)
- IT 561347-53-3
 RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
 (nucleotide sequence; human serum **albumin fusion**
 proteins for prolonged **shelf-life** of therapeutic proteins)
- IT 561350-18-3, 1: PN: WO03059934 SEQID: 1 unclaimed DNA 561350-19-4, 2:
 PN: WO03059934 SEQID: 2 unclaimed DNA 561350-20-7, 5: PN: WO03059934
 SEQID: 5 unclaimed DNA 561350-21-8, 6: PN: WO03059934 SEQID: 6 unclaimed
 DNA 561350-22-9, 7: PN: WO03059934 SEQID: 7 unclaimed DNA 561350-23-0,
 8: PN: WO03059934 SEQID: 8 unclaimed DNA 561350-24-1, 9: PN: WO03059934
 SEQID: 9 unclaimed DNA 561350-25-2 561350-26-3 561350-27-4
 561350-28-5 561350-29-6 561350-30-9 561350-31-0 561350-32-1
 561350-33-2 561350-34-3 561350-35-4 561350-36-5 561350-37-6
 561350-38-7 561350-39-8 561350-40-1 561350-41-2 561350-42-3
 561350-43-4 561350-44-5 561350-45-6 561350-46-7 561350-47-8
 561350-48-9 561351-02-8 561351-03-9 561351-04-0 561351-05-1
 561351-06-2 561351-07-3 561351-08-4 561351-09-5 561351-10-8

561351-11-9	561351-12-0	561351-13-1	561351-14-2	561351-15-3
561351-16-4	561351-17-5	561351-18-6	561351-19-7	561351-20-0
561351-21-1	561351-22-2	561351-23-3	561351-24-4	561351-25-5
561351-26-6	561351-27-7	561351-28-8	561351-29-9	561351-30-2
561351-31-3	561351-32-4	561351-33-5	561351-34-6	561351-35-7
561351-36-8	561351-37-9	561351-38-0	561351-39-1	561351-40-4
561351-41-5	561351-42-6	561351-43-7	561351-44-8	561351-45-9
561351-46-0	561351-47-1	561351-48-2	561351-49-3	561351-50-6
561351-51-7	561351-52-8	561351-53-9	561351-54-0	561351-55-1
561351-56-2	561351-57-3	561351-58-4	561351-59-5	561351-60-8
561351-61-9	561351-62-0	561351-63-1	561351-64-2	561351-65-3
561351-66-4	561351-67-5	561351-68-6	561351-69-7	561351-70-0
561351-71-1	561351-72-2	561351-73-3	561351-74-4	561351-75-5
561351-76-6	561351-77-7	561351-78-8	561351-79-9	561351-80-2
561351-81-3	561351-82-4	561351-83-5	561351-84-6	561351-85-7
561351-86-8	561351-88-0	561351-89-1	561351-90-4	561351-91-5
561351-92-6	561351-93-7	561351-94-8	561351-95-9	561351-96-0
561351-97-1	561351-98-2	561351-99-3	561352-00-9	561352-01-0
561352-02-1	561352-03-2	561352-04-3	561352-05-4	561352-06-5
561352-07-6	561352-08-7	561352-09-8	561352-10-1	561352-11-2
561352-12-3	561352-13-4	561352-14-5	561352-15-6	561352-16-7
561352-17-8	561352-18-9	561352-19-0	561352-20-3	561352-21-4
561352-22-5	561352-23-6	561352-24-7	561352-25-8	561352-26-9
561352-27-0	561352-28-1	561352-29-2	561352-30-5	561352-31-6
561352-32-7	561352-33-8	561352-34-9	561352-35-0	561352-37-2
561352-39-4	561352-41-8	561352-42-9	561352-43-0	561352-44-1
561352-45-2	561352-46-3	561352-47-4	561352-48-5	561352-49-6
561352-50-9	561352-58-7	561352-59-8	561352-60-1	561352-61-2
561352-62-3	561352-63-4	561352-64-5	561352-66-7	561352-67-8
561352-69-0	561352-71-4	561352-73-6	561352-75-8	561352-77-0
561352-80-5	561352-82-7	561352-83-8	561352-84-9	561352-85-0
561352-86-1	561352-87-2	561352-88-3	561352-89-4	561352-90-7
561352-91-8	561352-92-9	561352-93-0	561352-94-1	561352-95-2
561352-96-3	561352-97-4	561352-98-5	561352-99-6	561353-00-2
561353-01-3	561353-02-4	561353-03-5	561353-04-6	561353-05-7
561353-06-8	561353-07-9	561353-08-0	561353-09-1	561353-10-4
561353-11-5	561353-12-6	561353-13-7	561353-14-8	561353-15-9
561353-16-0	561353-17-1	561353-18-2	561354-10-7	561354-11-8
561354-12-9	561354-13-0	561354-14-1	561354-15-2	561354-16-3
561354-17-4	561354-18-5	561354-19-6	561354-20-9	561354-21-0

RL: PRP (Properties)

(unclaimed nucleotide sequence; **albumin fusion**
proteins for prolonged **shelf-life** of therapeutic
proteins)

IT	561354-22-1	561354-23-2	561354-24-3	561354-25-4	561354-26-5
	561354-27-6	561354-28-7	561354-29-8	561354-30-1	561354-31-2
	561354-32-3	561354-33-4	561354-34-5	561354-35-6	561354-36-7
	561354-37-8	561354-38-9	561354-39-0	561354-40-3	561354-41-4
	561354-42-5	561354-43-6	561354-44-7	561354-45-8	561354-46-9
	561354-47-0	561354-48-1	561354-49-2	561354-50-5	561354-51-6
	561354-52-7	561354-53-8	561354-54-9	561354-55-0	561354-56-1
	561354-57-2	561354-58-3	561354-59-4	561354-60-7	561354-61-8
	561354-62-9	561354-65-2	561354-66-3	561354-67-4	561354-68-5
	561354-69-6	561354-70-9	561354-71-0	561354-72-1	561354-73-2
	561354-74-3	561354-75-4	561354-76-5	561354-77-6	561354-78-7
	561354-79-8	561354-80-1	561354-81-2	561354-82-3	561354-83-4
	561354-84-5	561354-85-6	561354-86-7	561354-87-8	561354-92-5
	561354-93-6	561354-96-9	561354-97-0		

RL: PRP (Properties)

(unclaimed nucleotide sequence; **albumin fusion**
proteins for prolonged **shelf-life** of therapeutic
proteins)

IT	561350-49-0	561350-50-3	561350-51-4	561350-52-5	561350-53-6
----	-------------	-------------	-------------	-------------	-------------

561350-54-7	561350-55-8	561350-56-9	561350-57-0	561350-58-1
561350-59-2	561350-60-5	561350-61-6	561350-62-7	561350-63-8
561350-64-9	561350-65-0	561350-66-1	561350-67-2	561350-68-3
561350-69-4	561350-70-7	561350-71-8	561350-72-9	561350-73-0
561350-74-1	561350-75-2	561350-76-3	561350-77-4	561350-78-5
561350-79-6	561350-80-9	561350-81-0	561350-82-1	561350-83-2
561350-84-3	561350-85-4	561350-86-5	561350-87-6	561350-88-7
561350-89-8	561350-90-1	561350-91-2	561350-92-3	561350-93-4
561350-94-5	561350-95-6	561350-96-7	561350-97-8	561350-98-9
561350-99-0	561351-00-6	561351-01-7	561352-36-1	561352-38-3
561352-40-7	561352-51-0	561352-52-1	561352-53-2	561352-54-3
561352-55-4	561352-56-5	561352-57-6	561352-65-6	561352-68-9
561352-70-3	561352-72-5	561352-74-7	561352-76-9	561352-78-1
561352-79-2	561352-81-6	561353-19-3	561353-20-6	561353-21-7
561353-22-8	561353-23-9	561353-24-0	561353-25-1	561353-26-2
561353-27-3	561353-28-4	561353-29-5	561353-30-8	561353-31-9
561353-32-0	561353-33-1	561353-34-2	561353-35-3	561353-36-4
561353-37-5	561353-38-6	561353-39-7	561353-40-0	561353-41-1
561353-42-2	561353-43-3	561353-44-4	561353-45-5	561353-46-6
561353-47-7	561353-48-8	561353-49-9	561353-50-2	561353-51-3
561353-52-4	561353-53-5	561353-54-6	561353-55-7	561353-56-8
561353-57-9	561353-58-0	561353-59-1	561353-60-4	561353-61-5
561353-62-6	561353-63-7	561353-64-8	561353-65-9	561353-66-0
561353-67-1	561353-68-2	561353-69-3	561353-70-6	561353-71-7
561353-72-8	561353-73-9	561353-74-0	561353-75-1	561353-76-2
561353-77-3	561353-78-4	561353-79-5	561353-80-8	561353-81-9
561353-82-0	561353-83-1	561353-84-2	561353-85-3	561353-86-4
561353-87-5	561353-89-7	561353-90-0	561353-91-1	561353-92-2
561353-93-3	561353-94-4	561353-95-5	561353-96-6	561353-97-7
561353-98-8	561353-99-9	561354-00-5	561354-01-6	561354-02-7
561354-03-8	561354-04-9	561354-05-0	561354-06-1	561354-07-2
561354-08-3	561354-09-4	561354-63-0	561354-64-1	561354-88-9
561354-89-0	561354-90-3	561354-91-4	561354-94-7	561354-95-8

RL: PRP (Properties)

(unclaimed protein sequence; **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT 33017-11-7, Proinsulin C-peptide (human) 40958-31-4, Somatostatin (sheep reduced) 82177-09-1 85482-68-4 85734-71-0 122024-47-9
 125677-89-6 130912-02-6 131748-18-0 131748-19-1 157654-59-6
 166980-40-1 170098-75-6 192503-43-8 247166-37-6 367273-47-0
 367273-48-1 477953-25-6 477953-26-7 477953-27-8 477953-28-9
 477953-29-0 477953-30-3 477953-31-4 477953-32-5 477953-33-6
 477953-34-7 477953-35-8 478188-11-3 478188-13-5 561304-79-8
 561304-80-1 561304-82-3 561304-83-4 561304-84-5 561304-85-6
 561304-86-7 561304-87-8 561304-88-9 561304-92-5 561304-95-8

RL: PRP (Properties)

(unclaimed sequence; **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

L66 ANSWER 3 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2003:300832 HCAPLUS
 DN 138:326508
 ED Entered STN: 18 Apr 2003
 TI **Albumin fusion** proteins with therapeutic proteins for improved **shelf-life**
 IN Rosen, Craig A.; Hasseltine, William A.
 PA Human Genome Sciences, Inc., USA
 SO PCT Int. Appl., 457 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K

CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 3, 15

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003030821	A2	20030417	WO 2002-US31794	20021004
	WO 2003030821	A3	20031211		
				W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG	
PRAI	US 2001-327281P	P	20011005		
AB	The present invention encompasses fusion proteins of albumin with various therapeutic proteins. Therapeutic proteins may be stabilized to extend the shelf-life , and/or to retain the therapeutic protein's activity for extended periods of time in solution, in vitro and/or in vivo, by genetically or chemical fusing or conjugating the therapeutic protein to albumin or a fragment or variant of albumin . Use of albumin fusion proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the albumin fusion proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the albumin fusion proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired therapeutic protein may be inserted for expression of the albumin fusion proteins in yeast (pPPC0005) and mammalian cells (pC4:HSA). Yeast-derived signal sequences from <i>Saccharomyces cerevisiae</i> invertase SUC2 gene, or the stanniocalcin or native human serum albumin signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the fusion product of human growth hormone with residues 1-387 of human serum albumin retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37°, whereas recombinant human growth hormone used as control lost its biol. activity in the first week. Although the potency of the albumin fusion proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. stability results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical compns. Comprising albumin fusion proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using albumin fusion proteins of the invention.				
ST	albumin fusion therapeutic protein shelflife				
IT	Drug delivery systems Gene therapy Human Molecular cloning (albumin fusion proteins with therapeutic proteins for improved shelf-life)				
IT	Fusion proteins (chimeric proteins) Interferons RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)				

- (**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Signal peptides
 - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 - (**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Peptides, biological studies
 - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 - (linkers; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Animal cell
 - (mammalian, **recombinant** expression host; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Plasmid vectors
 - (pC4:HSA, for mammalian cell expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Plasmid vectors
 - (pPPC0005, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Plasmid vectors
 - (pScCHSA, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Plasmid vectors
 - (pScNHSA, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Linking agents
 - (peptide; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Saccharomyces cerevisiae
 - Yeast
 - (**recombinant** expression host; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT **Albumins, biological studies**
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (serum; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Genetic element
 - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 - (signal sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Antibodies
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (single chain; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (therapeutic; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT **Interferons**
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(α ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 9002-72-6DP, Growth hormone, **fusion** proteins with **albumin**
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 511566-72-6DP, **Albumin** (human blood serum), full-length or subfragment **fusion** proteins
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (amino acid sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 511566-73-7
 RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
 (nucleotide sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 511603-12-6 511603-13-7 511603-14-8 511603-15-9 511603-16-0
 511603-17-1 511603-18-2 511603-19-3 511603-20-6 511603-21-7
 511603-22-8 511603-23-9 511603-24-0 511603-25-1 511603-26-2
 511603-27-3 511603-28-4 511603-29-5 511603-30-8 511603-31-9
 511603-32-0 511603-33-1 511603-34-2 511603-35-3 511603-36-4
 511603-37-5 511603-38-6 511603-39-7 511603-40-0 511603-41-1
 511603-42-2 511603-43-3 511603-44-4 511603-45-5 511603-46-6
 511603-47-7 511603-48-8 511603-49-9 511603-50-2 511603-51-3
 511603-52-4 511603-53-5 511603-54-6 511603-55-7 511603-56-8
 511603-57-9 511603-58-0 511603-59-1 511603-60-4 511603-61-5
 511603-62-6 511603-63-7 511603-64-8 511603-65-9 511603-66-0
 511603-67-1 511603-68-2 511603-69-3
 RL: PRP (Properties)
 (unclaimed nucleotide sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 122024-47-9 131748-18-0 367273-46-9 367273-47-0 367273-48-1
 RL: PRP (Properties)
 (unclaimed sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

L66 ANSWER 4 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2003:125793 HCAPLUS
 DN 138:297265
 ED Entered STN: 19 Feb 2003
 TI An **IFN- β -Albumin Fusion**
 Protein That Displays Improved Pharmacokinetic and Pharmacodynamic Properties in Nonhuman Primates
 AU Sung, Cynthia; Nardelli, Bernadetta; LaFleur, David W.; Blatter, Erich; Corcoran, Marta; Olsen, Henrik S.; Birse, Charles E.; Pickeral, Oxana K.; Zhang, Junli; Shah, Devanshi; Moody, Gordon; Gentz, Solange; Beebe, Lisa; Moore, Paul A.
 CS Human Genome Sciences, Inc., Rockville, MD, 20850, USA
 SO Journal of Interferon and Cytokine Research (2003), 23(1), 25-36
 CODEN: JICREFJ; ISSN: 1079-9907
 PB Mary Ann Liebert, Inc.
 DT Journal
 LA English
 CC 1-7 (Pharmacology)
 Section cross-reference(s): 15
 AB The long half-life and stability of human serum **albumin** (HSA) make it an attractive candidate for **fusion** to short-lived therapeutic proteins. Albuferon beta (Human Genome Sciences [HGS], Inc., Rockville, MD) is a novel **recombinant** protein derived from a

gene fusion of interferon- β (IFN- β) and HSA. In vitro, Albuferon beta displays antiviral and antiproliferative activities and triggers the IFN-stimulated response element (ISRE) signal transduction pathway. Array anal. of 5694 independent genes in Daudi-treated cells revealed that Albuferon beta and IFN- β induce the expression of an identical set of 30 genes, including 9 previously not identified. In rhesus monkeys administered a dose of 50 μ g/kg i.v. or s.c. or 300 μ g/kg s.c., Albuferon beta demonstrated favorable pharmacokinetic properties. S.c. bioavailability was 87%, plasma clearance at 4.7-5.7 mL/h/kg was approx. 140-fold lower than that of IFN- β , and the terminal half-life was 36-40 h compared with 8 h for IFN-. Importantly, Albuferon beta induced sustained increases in serum neopterin levels and 2',5'-oligoadenylate synthetase (2',5'-OAS) mRNA expression. At a molar dose equivalent to one-half the dose of IFN- β , Albuferon beta elicited comparable neopterin responses and significantly higher 2',5'-OAS mRNA levels in rhesus monkeys. The enhanced in vivo pharmacol. properties of IFN-. beta. when fused to serum albumin suggest a clin. opportunity for improved IFN- β therapy.

ST **interferon beta albumin fusion**

protein albuferon beta pharmacokinetic pharmacodynamic

IT **Fusion proteins (chimeric proteins)**

RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(IFN- β -HSA; IFN- β -

albumin fusion protein with retained biol. activities and improved pharmacokinetic and pharmacodynamic properties of IFN- β in primates)

IT Antiviral agents

Human

Macaca mulatta

Pharmacodynamics

Pharmacokinetics

Signal transduction, biological

(IFN- β -**albumin fusion**

protein with retained biol. activities and improved pharmacokinetic and pharmacodynamic properties of IFN- β in primates)

IT Genetic element

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(ISRE (interferon-stimulated response element); IFN-

- β -**albumin fusion** protein with

retained biol. activities and improved pharmacokinetic and pharmacodynamic properties of IFN- β in primates)

IT Transcriptional regulation

(activation; IFN- β -**albumin**

fusion protein with retained biol. activities and improved pharmacokinetic and pharmacodynamic properties of IFN- β in primates)

IT Cell proliferation

(inhibition; IFN- β -**albumin**

fusion protein with retained biol. activities and improved pharmacokinetic and pharmacodynamic properties of IFN- β in primates)

IT **Albumins, biological studies**

RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(serum, human, **fusion** protein with IFN- β ; IFN- β -**albumin**

fusion protein with retained biol. activities and improved pharmacokinetic and pharmacodynamic properties of IFN- β in primates)

IT **Interferons**

RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (β , **fusion protein with albumin**;
IFN- β -albumin fusion protein
 with retained biol. activities and improved pharmacokinetic and pharmacodynamic properties of **IFN- β** in primates)

IT 507485-69-0P, **Albuferon beta**

RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (**IFN- β -HSA; IFN- β -**
albumin fusion protein with retained biol. activities and improved pharmacokinetic and pharmacodynamic properties of **IFN- β** in primates)

IT 2009-64-5, **Neopterin 69106-44-1, 2',5'-Oligoadenylylate synthetase**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (**IFN- β -albumin fusion**
 protein with retained biol. activities and improved pharmacokinetic and pharmacodynamic properties of **IFN- β** in primates)

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Brumell, J; J Immunol 1999, V163, P3388 HCPLUS
- (2) Chuang, V; Pharm Res 2002, V19, P569
- (3) Durelli, L; Lancet 2002, V359, P1453 HCPLUS
- (4) Eisen, M; Proc Natl Acad Sci USA 1998, V95, P14863 HCPLUS
- (5) Fierlbeck, G; J Interferon Cytokine Res 1996, V16, P777 MEDLINE
- (6) Fine, H; Clin Cancer Res 1997, V3, P381 HCPLUS
- (7) Fukutomo, T; J Hepatol 2001, V34, P100
- (8) Glue, P; Clin Pharmacol Ther 2000, V68, P556 HCPLUS
- (9) Grace, M; J Interferon Cytokine Res 2001, V21, P1103 HCPLUS
- (10) Guterman, J; Proc Natl Acad Sci USA 1994, V91, P1198 HCPLUS
- (11) Imaizumi, T; J Leukocyte Biol 2002, V72, P486 HCPLUS
- (12) Jacobs, L; N Engl J Med 2000, V343, P898 HCPLUS
- (13) Karsan, A; Blood 1996, V87, P3089 HCPLUS
- (14) Kho, C; J Biol Chem 1997, V272, P13426 HCPLUS
- (15) Lafleur, D; J Biol Chem 2001, V276, P39765 HCPLUS
- (16) Leaman, D; J Biol Chem 2002, V277, P28504 HCPLUS
- (17) Lindsay, K; Hepatology 2001, V34, P395 HCPLUS
- (18) Lukashok, S; J Virol 2000, V74, P4705 HCPLUS
- (19) Maeyer, E; The Cytokine Handbook, 3rd ed 1998, P491
- (20) Marques, J; Thromb Haemost 2001, V86, P902 HCPLUS
- (21) Osborn, B; Eur J Pharmacol 2002, V456, P149 HCPLUS
- (22) Osborn, B; J Pharmacol Exp Ther 2002, V303, P540 HCPLUS
- (23) Paty, D; Neurology 1993, V43, P662 MEDLINE
- (24) Pellegrini, S; Mol Cell Biol 1989, V9, P4605 HCPLUS
- (25) Pepinsky, R; J Pharmacol Exp Ther 2001, V297, P1059 HCPLUS
- (26) Peters, T; All About Albumin 1996
- (27) Pferrer, L; Cancer Res 1998, V58, P2489
- (28) Prisms Study Group; Lancet 1998, V352, P1498
- (29) Prisms Study Group and the University of British Columbia MS/MRI Analysis Group; Neurology 2001, V56, P1628
- (30) Runkel, L; Pharm Res 1998, V15, P641 HCPLUS
- (31) Salmon, P; J Interferon Cytokine Res 1996, V16, P759 HCPLUS
- (32) Schindler, C; Annu Rev Biochem 1995, V64, P621 HCPLUS
- (33) Silva, D; J Interferon Cytokine Res 2002, V22, P173
- (34) Soh, J; J Biol Chem 1994, V269, P18102 HCPLUS

- (35) Stark, G; Annu Rev Biochem 1998, V67, P227 HCAPLUS
 (36) Suginoshita, Y; J Pharmacol Exp Ther 2001, V298, P805 HCAPLUS
 (37) Syed, S; Blood 1997, V89, P3243 HCAPLUS
 (38) Uze, G; Cell 1990, V60, P225 HCAPLUS
 (39) Williams, G; J Interferon Cytokine Res 1998, V18, P967 HCAPLUS
 (40) Witt, P; Interferon Therapy of Multiple Sclerosis 1997, P77 HCAPLUS
 (41) Zannettino, A; Blood 1998, V92, P2613 HCAPLUS

L66 ANSWER 5 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2002:834389 HCAPLUS
 DN 137:304506
 ED Entered STN: 03 Nov 2002
 TI Pharmacokinetic and pharmacodynamic studies of a human serum
albumin-interferon- α fusion
 protein in cynomolgus monkeys
 AU Osborn, Blaire L.; Olsen, Henrik S.; Nardelli, Bernardetta; Murray, James
 H.; Zhou, Joe X. H.; Garcia, Andrew; Moody, Gordon; Zaritskaya, Liubov S.;
 Sung, Cynthia
 CS Human Genome Sciences, Inc., Rockville, MD, USA
 SO Journal of Pharmacology and Experimental Therapeutics (2002), 303(2),
 540-548
 CODEN: JPETAB; ISSN: 0022-3565
 PB American Society for Pharmacology and Experimental Therapeutics
 DT Journal
 LA English
 CC 1-7 (Pharmacology)
 Section cross-reference(s): 15
 AB **Interferon- α (IFN- α)**
 is indicated for the treatment of certain viral **infections**
 including hepatitis B and C, and cancers such as melanoma. The short
 circulating half-life of unmodified **IFN- α** makes
 frequent dosing (daily or three times weekly) over an extended period
 (6-12 mo or more) necessary. To improve the pharmacokinetics of
IFN- α and decrease dosing frequency, **IFN- α**
 was **fused** to human serum **albumin**
 producing a new protein, Albuferon. In vitro comparisons of Albuferon and
IFN- α showed similar antiviral and
 antiproliferative activities, although Albuferon was less potent on a
 molar basis than **IFN- α** . Pharmacokinetic and
 pharmacodynamic properties of the **fusion** protein were enhanced
 in monkeys. After a single i.v. injection (30 μ g/kg) clearance was 0.9
 mL/h/kg, and the terminal half-life was 68 h. After 30 μ g/kg s.c.
 injection, apparent clearance (clearance divided by bioavailability) was
 1.4 mL/h/kg, the terminal half-life was 93 h, and bioavailability was 64%.
 The rate of clearance of Albuferon was approx. 140-fold slower, and the
 half-life 18-fold longer, than for **IFN- α** given
 by the s.c. route in other monkey studies. Sera from Albuferon-treated
 monkeys demonstrated dose-related antiviral activity for \geq 8 days
 based on an in vitro bioassay, whereas antiviral activity from **IFN- α**
 -treated animals was only slightly elevated relative to
 vehicle on day 0. Significant increases in 2',5'-oligoadenylate
 synthetase mRNA relative to **IFN- α** - or
 vehicle-treated animals were maintained for \geq 10 days after s.c.
 dosing. The improved pharmacokinetics of Albuferon are accompanied by an
 improved pharmacodynamic response suggesting that Albuferon may offer the
 benefits of less frequent dosing and a potentially improved efficacy
 profile compared with **IFN- α** .
 ST Albuferon **interferon** antiviral antiproliferative
 pharmacokinetics pharmacodynamics
 IT Antiviral agents
 Cytotoxic agents
 Human
 Macaca irus

Pharmacodynamics

Pharmacokinetics

(pharmacokinetic and pharmacodynamic studies of a human serum
albumin-interferon- α fusion
protein in cynomolgus monkeys)

IT **Albumins, biological studies**

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(serum, **fusion** protein with **interferon-**
 α ; pharmacokinetic and pharmacodynamic studies of a human serum
albumin-interferon- α fusion protein in cynomolgus monkeys)

IT **Interferons**

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α , **fusion** protein with human serum
albumin; pharmacokinetic and pharmacodynamic studies of a human serum
albumin-interferon- α fusion protein in cynomolgus monkeys)

IT 69106-44-1, 2',5'-Oligoadenylate synthetase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacokinetic and pharmacodynamic studies of a human serum
albumin-interferon- α fusion
protein in cynomolgus monkeys)

IT 98530-12-2, Intron-A 472960-22-8, Albuferon

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetic and pharmacodynamic studies of a human serum
albumin-interferon- α fusion
protein in cynomolgus monkeys)

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Ahmed, A; Clin Liver Dis 1999, V3, P757 MEDLINE
- (2) Anon; Med Lett Drugs Ther 1997, V39(1006), P69
- (3) Bailon, P; Bioconjug Chem 2001, V12, P195 HCPLUS
- (4) Chinery, S; Curr Genet 1989, V1, P21
- (5) Collins, J; Cancer Drug Deliv 1985, V2, P247 HCPLUS
- (6) Damen, M; Scand J Gastroenterol 2001, V36, P97 HCPLUS
- (7) Davis, G; N Engl J Med 1989, V321, P1501 MEDLINE
- (8) Fischer, T; Br J Haematol 1996, V92, P595 HCPLUS
- (9) Food and Drug Administration; Toxicologist's Review 2000, BLA 99-1488
- (10) Foster, G; Semin Liver Dis 1997, V17, P287 HCPLUS
- (11) Fried, M; Semin Liver Dis 1995, V15, P82 MEDLINE
- (12) Glue, P; Clin Pharmacol Ther 2000, V68, P556 HCPLUS
- (13) Hinchliffe, E; EP 0286424 1994 HCPLUS
- (14) Hinchliffe, E; US 5637504 1997 HCPLUS
- (15) Hu, K; J Viral Hepatitis 2001, V8, P1 MEDLINE
- (16) Kramer, M; J Interferon Res 1983, V3, P425 HCPLUS
- (17) LaFleur, D; J Biol Chem 2001, V276, P39765 HCPLUS
- (18) Maeyer, E; The Cytokine Handbook, 3rd ed 1998, P491
- (19) Mordini, J; Pharm Res (NY) 1991, V8, P1351 HCPLUS
- (20) Moritz, T; Mol Biother 1992, V4, P97 MEDLINE
- (21) Motzer, R; J Clin Oncol 2001, V19, P1312 HCPLUS
- (22) Murashima, S; J Med Virol 2000, V62, P185 HCPLUS
- (23) Naik, D; Applied Multivariate Statistics with SAS Software, 2nd ed 1999
- (24) Perry, C; Drugs 2001, V61, P2263 HCPLUS
- (25) Peters, T; All About Albumin 1996
- (26) Pfeifer, L; Cancer Res 1998, V58, P2489
- (27) Rubinstein, S; J Virol 1981, V37, PP755
- (28) Runkel, L; J Biol Chem 1998, V273, P8003 HCPLUS
- (29) Syed, S; Blood 1997, V89, P3243 HCPLUS
- (30) Talpaz, M; Blood 2001, V98, P1708 HCPLUS
- (31) Thevenot, T; J Viral Hepatitis 2001, V8, P48 MEDLINE

- (32) Tine, F; J Hepatol 1991, V13, P192 MEDLINE
 (33) Trown, P; Cancer 1986, V57, P1648 HCAPLUS
 (34) Wills, R; J Interferon Res 1984, V4, P399 HCAPLUS
 (35) Yeh, P; Proc Natl Acad Sci USA 1992, V89, P1904 HCAPLUS

L66 ANSWER 6 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2001:781112 HCAPLUS
 DN 135:348852
 ED Entered STN: 26 Oct 2001
 TI **Albumin fusion** proteins with therapeutic proteins for improved **shelf-life**
 IN Rosen, Craig A.; Haseltine, William A.
 PA Human Genome Sciences, Inc., USA
 SO PCT Int. Appl., 394 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM C12N015-00
 CC 63-3 (Pharmaceuticals)
 Section cross-reference(s): 3, 15
 FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001079480	A1	20011025	WO 2001-US11991	20010412
	WO 2001079480	C2	20030109		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1276856	A1	20030122	EP 2001-937179	20010412
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003125247	A1	20030703	US 2001-833041	20010412
	US 2003171267	A1	20030911	US 2001-833117	20010412
	JP 2003530852	T2	20031021	JP 2001-577463	20010412
	US 2003199043	A1	20031023	US 2001-832501	20010412
	US 2003219875	A1	20031127	US 2001-833118	20010412
	US 2004010134	A1	20040115	US 2001-833245	20010412
PRAI	US 2000-229358P	P	20000412		
	US 2000-199384P	P	20000425		
	US 2000-256931P	P	20001221		
	WO 2001-US11991	W	20010412		
AB	The present invention encompasses fusion proteins of albumin with various therapeutic proteins. Therapeutic proteins may be stabilized to extend the shelf-life , and/or to retain the therapeutic protein's activity for extended periods of time in solution, in vitro and/or in vivo, by genetically or chemical fusing or conjugating the therapeutic protein to albumin or a fragment or variant of albumin . Use of albumin fusion proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the albumin fusion proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the albumin fusion proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired				

therapeutic protein may be inserted for expression of the **albumin fusion** proteins in yeast (pPPC0005) and mammalian cells (pC4:HSA). Yeast-derived signal sequences from *Saccharomyces cerevisiae* invertase SUC2 gene, or the stanniocalcin or native human serum **albumin** signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the **fusion** product of human growth hormone with residues 1-387 of human serum **albumin** retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37°, whereas **recombinant** human growth hormone used as control lost its biol. activity in the first week. Although the potency of the **albumin fusion** proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. stability results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical compns. comprising **albumin fusion** proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using **albumin fusion** proteins of the invention.

- ST **albumin fusion** therapeutic protein **shelflife**
- IT Receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(4-1BB; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Cytokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(BAFF; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Cytokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(DR4 (death receptor 4); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Cytokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(DR5 (death receptor 5); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Cytokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MIF-1 (myeloid progenitor inhibitory factor 1); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Steroid receptors
Thyroid hormone receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TR (thyroid/stEROID hormone receptor), 11; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Steroid receptors
Thyroid hormone receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TR (thyroid/stEROID hormone receptor), 12; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Steroid receptors
Thyroid hormone receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TR (thyroid/stEROID hormone receptor), 13; **albumin**

- fusion proteins with therapeutic proteins for improved
shelf-life)
- IT Steroid receptors
Thyroid hormone receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TR (thyroid/steroid hormone receptor), 14; **albumin**
fusion proteins with therapeutic proteins for improved
shelf-life)
- IT Steroid receptors
Thyroid hormone receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TR (thyroid/steroid hormone receptor), 16; **albumin**
fusion proteins with therapeutic proteins for improved
shelf-life)
- IT Steroid receptors
Thyroid hormone receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TR (thyroid/steroid hormone receptor), 8; **albumin**
fusion proteins with therapeutic proteins for improved
shelf-life)
- IT Steroid receptors
Thyroid hormone receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TR2 (thyroid/steroid hormone receptor 2); **albumin**
fusion proteins with therapeutic proteins for improved
shelf-life)
- IT Steroid receptors
Thyroid hormone receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TR3 (thyroid/steroid hormone receptor 3); **albumin**
fusion proteins with therapeutic proteins for improved
shelf-life)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TRAIL (tumor necrosis factor-related apoptosis-inducing ligand);
albumin fusion proteins with therapeutic proteins for
improved **shelf-life**)
- IT Cytokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TRAIL, 4; **albumin fusion** proteins with therapeutic
proteins for improved **shelf-life**)
- IT Cytokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TRAIL, 6; **albumin fusion** proteins with therapeutic
proteins for improved **shelf-life**)
- IT Cytokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TRAIL-R3; **albumin fusion** proteins with therapeutic
proteins for improved **shelf-life**)
- IT Drug delivery systems
Gene therapy
Molecular cloning
(**albumin fusion** proteins with therapeutic proteins
for improved **shelf-life**)

- IT Cell adhesion molecules
 - Cytokines
 - Enzymes, biological studies
 - Fas antigen
 - Fas ligand
 - Fusion proteins (chimeric proteins)**
 - Growth factors, animal
 - Interferons**
 - Synthetic gene
 - Tumor necrosis factor receptors
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (apoptosis-regulating, AIM-2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Cytokines
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (endokine; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Signal peptides
 - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 - (for improved secretion in yeast or mammalian cells; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT **Interferons**
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (keratinocyte-derived; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Animal cell
 - (mammalian, **recombinant** expression host; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Plasmid vectors
 - (pC4:HSA, for mammalian cell expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Plasmid vectors
 - (pPPC0005, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Plasmid vectors
 - (pScCHSa, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Plasmid vectors
 - (pScNHSA, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Saccharomyces cerevisiae
 - Yeast
 - (**recombinant** expression host; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT **Albumins, biological studies**
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic

- use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (serum; **albumin fusion** proteins with therapeutic
 proteins for improved **shelf-life**)
- IT Genetic element
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (signal sequence, for improved secretion in yeast or mammalian cells;
albumin fusion proteins with therapeutic proteins for
 improved **shelf-life**)
- IT Antibodies
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic
 use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (single chain; **albumin fusion** proteins with
 therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic
 use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (therapeutic; **albumin fusion** proteins with
 therapeutic proteins for improved **shelf-life**)
- IT **Interferons**
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic
 use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (α ; **albumin fusion** proteins with
 therapeutic proteins for improved **shelf-life**)
- IT Chemokine receptors
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic
 use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (β chemokine receptor CCR5; **albumin fusion**
 proteins with therapeutic proteins for improved **shelf-**
life)
- IT Tumor necrosis factors
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic
 use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (γ ; **albumin fusion** proteins with therapeutic
 proteins for improved **shelf-life**)
- IT Tumor necrosis factors
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic
 use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (δ ; **albumin fusion** proteins with therapeutic
 proteins for improved **shelf-life**)
- IT 189460-40-0P, Connective tissue growth factor
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic
 use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (2 and 4; **albumin fusion** proteins with therapeutic
 proteins for improved **shelf-life**)
- IT 9001-84-7P, Phospholipase A2
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic
 use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (T-cell lymphoma lipoprotein-associated; **albumin fusion**
 proteins with therapeutic proteins for improved **shelf-**
life)
- IT 9002-67-9P, Luteinizing hormone 9002-68-0P, FSH 9002-72-6P, Growth
 hormone 9004-10-8P, Insulin, biological studies 11096-26-7P,
 Erythropoietin 67763-96-6P, Insulin-like growth factor 1 83869-56-1P,
 GM-CSF 124861-55-8P, Proteinase inhibitor, **TIMP-2**
 127464-60-2P, Vascular endothelial growth factor **140208-24-8P**,
 Proteinase inhibitor, **TIMP-1** 143011-72-7P, G-CSF
 145809-21-8P, Proteinase inhibitor, **TIMP-3** 148348-15-6P,
 Fibroblast growth factor 7 171758-70-6P, Keratinocyte growth factor 2
 186207-03-4P, Proteinase inhibitor, **TIMP-4** 205944-50-9P,
 Osteoprotegerin 207621-35-0P, Osteoprotegerin ligand 244019-42-9P,
 Vascular endothelial growth factor 2
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic

use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (albumin fusion proteins with therapeutic proteins
 for improved shelf-life)

IT 127361-02-8DP, **Albumin** (human blood serum clone HSA-II/HSA-I-A
 protein moiety reduced), full-length or subfragment **fusion**
 products
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic
 use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (nucleotide sequence; albumin fusion proteins with
 therapeutic proteins for improved shelf-life)

IT 155945-98-5, PN: US5962255 SEQID: 59 unclaimed DNA 156163-00-7
 167728-69-0 167728-70-3 167728-71-4 167728-72-5 167728-73-6
 167731-70-6 167731-74-0, PN: US5962255 SEQID: 56 unclaimed DNA
 167731-75-1, PN: US5962255 SEQID: 57 unclaimed DNA 167731-76-2, PN:
 US5962255 SEQID: 58 unclaimed DNA 167731-77-3, PN: US5962255 SEQID: 60
 unclaimed DNA 167731-78-4, PN: US5962255 SEQID: 61 unclaimed DNA
 167731-79-5 167731-80-8 167731-81-9 167732-10-7 167732-11-8, PN:
 US5962255 SEQID: 551 unclaimed DNA 167732-12-9 167732-13-0
 167732-14-1, PN: US5962255 SEQID: 554 unclaimed DNA 167732-15-2, PN:
 US5962255 SEQID: 555 unclaimed DNA 167732-16-3 167732-17-4
 167732-18-5 167732-19-6, PN: US5962255 SEQID: 98 unclaimed DNA
 167732-20-9, PN: US5962255 SEQID: 572 unclaimed DNA 167732-21-0
 167732-22-1, PN: US5962255 SEQID: 574 unclaimed DNA 195164-37-5
 217893-77-1, GenBank A63614 217893-78-2, GenBank A63615 217893-79-3,
 GenBank A63616 217893-80-6, GenBank A63617 217893-81-7, GenBank A63618
 217893-82-8, GenBank A63619 217893-83-9, GenBank A63620 217893-84-0,
 GenBank A63621 217893-85-1, GenBank A63622 217893-86-2, GenBank A63624
 217893-89-5, GenBank A63627 217893-90-8, GenBank A63628 217893-91-9,
 GenBank A63629 217893-92-0, GenBank A63630 367319-52-6 367319-53-7
 367319-54-8 367319-55-9 367319-56-0 367319-57-1 367319-58-2
 367319-59-3 367319-60-6 367319-61-7 367319-62-8 367319-63-9
 367319-64-0 367319-65-1 367319-66-2
 RL: PRP (Properties)
 (unclaimed nucleotide sequence; albumin fusion
 proteins with therapeutic proteins for improved shelf-
 life)

IT 173586-11-3 221879-28-3 222614-92-8 352583-76-7, Protein (human
 clone 785CIP2B_67) 370649-84-6 370649-85-7
 RL: PRP (Properties)
 (unclaimed protein sequence; albumin fusion
 proteins with therapeutic proteins for improved shelf-
 life)

IT 122024-47-9 131748-18-0 244008-03-5, PN: WO9947540 SEQID: 3 unclaimed
 DNA 244008-06-8, PN: WO9947540 SEQID: 4 unclaimed DNA 244008-07-9, PN:
 WO9947540 SEQID: 5 unclaimed DNA 244008-08-0, PN: WO9947540 SEQID: 6
 unclaimed DNA 244008-09-1, PN: WO9947540 SEQID: 7 unclaimed DNA
 244008-12-6, 8: PN: WO0183510 SEQID: 8 unclaimed DNA 244008-13-7, PN:
 WO9947540 SEQID: 9 unclaimed DNA 244008-14-8, PN: WO9947540 SEQID: 10
 unclaimed DNA 367273-46-9 367273-47-0 367273-48-1 370598-71-3
 370649-86-8
 RL: PRP (Properties)
 (unclaimed sequence; albumin fusion proteins with
 therapeutic proteins for improved shelf-life)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE
 (1) Delta Biotechnology Limited; EP 0322094 A1 1989 HCPLUS
 (2) Delta Biotechnology Limited; WO 9523857 A1 1995 HCPLUS

L66 ANSWER 7 OF 29 HCPLUS COPYRIGHT 2004 ACS on STN

AN 2001:781079 HCPLUS

DN 135:348851

ED Entered STN: 26 Oct 2001

TI **Albumin fusion** proteins with therapeutic proteins for

improved shelf-life

IN Rosen, Craig A.; Haseltine, William A.
 PA Human Genome Sciences, Inc, USA
 SO PCT Int. Appl., 606 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C12N

CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 3, 15

FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001079444	A2	20011025	WO 2001-US12013	20010412
	WO 2001079444	A3	20020523		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001074809	A5	20011020	AU 2001-74809	20010412
	EP 1278544	A2	20030129	EP 2001-941457	20010412
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003125247	A1	20030703	US 2001-833041	20010412
	US 2003171267	A1	20030911	US 2001-833117	20010412
	JP 2003530847	T2	20031021	JP 2001-577428	20010412
	US 2003199043	A1	20031023	US 2001-832501	20010412
	US 2003219875	A1	20031127	US 2001-833118	20010412
	US 2004010134	A1	20040115	US 2001-833245	20010412
PRAI	US 2000-229358P	P	20000412		
	US 2000-199384P	P	20000425		
	US 2000-256931P	P	20001221		
	WO 2001-US12013	W	20010412		

AB The present invention encompasses **fusion** proteins of **albumin** with various therapeutic proteins. Therapeutic proteins may be stabilized to extend the **shelf-life**, and/or to retain the therapeutic protein's activity for extended periods of time in solution, *in vitro* and/or *in vivo*, by genetically or chemical **fusing** or conjugating the therapeutic protein to **albumin** or a fragment or variant of **albumin**. Use of **albumin fusion** proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the **albumin fusion** proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the **albumin fusion** proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired therapeutic protein may be inserted for expression of the **albumin fusion** proteins in yeast (pPPC0005) and mammalian cells (pC4:HSA). Yeast-derived signal sequences from *Saccharomyces cerevisiae* invertase SUC2 gene, or the stanniocalcin or native human serum **albumin** signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the **fusion** product of human growth hormone with residues 1-387 of human serum **albumin** retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37°, whereas **recombinant** human growth hormone used as

control lost its biol. activity in the first week. Although the potency of the **albumin fusion** proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. stability results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical compns. comprising **albumin fusion** proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using **albumin fusion** proteins of the invention.

- ST **albumin fusion therapeutic protein shelflife**
- IT Chemokines
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (1-309; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Bone morphogenetic proteins
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (11; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Bone morphogenetic proteins
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (12; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Bone morphogenetic proteins
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (15; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Bone morphogenetic proteins
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (17; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Bone morphogenetic proteins
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (18; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Interleukins
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (19; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Bone morphogenetic proteins
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Interleukins
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (21; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Bone morphogenetic proteins
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (331D5; **albumin fusion** proteins with therapeutic

- IT proteins for improved **shelf-life**)
 - Bone morphogenetic proteins
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (3; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
 - Receptors
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (4-1BB; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
 - Bone morphogenetic proteins
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (4; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
 - Bone morphogenetic proteins
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (5; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
 - Chemokines
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (61164; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
 - Bone morphogenetic proteins
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (6; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
 - Bone morphogenetic proteins
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (7; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
 - Bone morphogenetic proteins
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (9; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
 - Platelet-derived growth factors
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (AA; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
 - Proteins, specific or class
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (ACRP-30; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
 - Chemokines
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (ADEC (adenoid expressed chemokine); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
 - Interleukins
 - RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (AGF; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
 - Proteins, specific or class

- RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (APM-1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (Act-2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Platelet-derived growth factors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (BB; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (BCMA; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Platelet-derived growth factors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (Bv-sis; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (C-C, 2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (C-C, 3; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (C-C, DGWCC; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (C-C, DVic-1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (C-C, ELC; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (C-C, HCC-1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (C-C, IBICK; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (C-C, ILINCK; **albumin fusion** proteins with

- therapeutic proteins for improved **shelf-life**)
- IT Chemokines
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (C-C, SLC (secondary lymphoid chemokine); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (C-C, STCP-1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (C-X-C, 3; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (C-X-C; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (C10; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Troponins
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (C; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (CC3; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (CCF18; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (CCR2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT CD antigens
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (CD27; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Glycoproteins, specific or class
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (CD40-L (antigen CD40 ligand); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (CTAP-III (connective tissue activating protein III); **albumin fusion** proteins with therapeutic proteins for improved

- shelf-life)
- IT Antigens
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (CTLA-8; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT Chemokine receptors
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (CXCR3; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT Proteins, specific or class
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (Cerebus; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT Proteins, specific or class
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (Chr19Kine; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT Platelet-derived growth factors
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (D; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT Cytokine receptors
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (DR3 (death receptor 3); **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT Proteins, specific or class
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (EDAR; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT Interleukins
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (EDIRF I protein; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT Chemokines
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (EEC (eosinophil expressed chemokine); **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT Proteins, specific or class
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (ENA-78 (epithelial neutrophil activating protein-78); **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT Hemopoietins
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (FLT3 ligand; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT Chemokines
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (HCC-1; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)

- IT Troponins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(I; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(L105-7; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(LVEC-1 (liver expressed chemokine 1); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(LVEC-2 (liver expressed chemokine 2); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Lyn-1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M110; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M11A; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MACK (mammary associated chemokine); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MCP-3 α and MCP-3 β ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MCP-4; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MCP-4; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MCPP (monocyte chemotactic proprotein); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

- (MDC (macrophage-derived chemokine); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Monokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MIG (monokine induced by γ - **interferon**);
albumin fusion proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MIG- β ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Interleukins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MIRAP; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MP52; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NOGO-66; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NOGO-A; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NOGO-B; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NOGO-C; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Antigens
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(OX-40; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PF4; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PGBC (pituitary expressed chemokine); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

- (RANTES; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(SISD; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(SLC (secondary lymphoid tissue chemokine); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Troponins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(T; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TAC1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Cytokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TARC (thymus and activation regulated cytokine); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TMEC (T cell mixed lymphocyte reaction expressed chemokine); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Tarc; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Tim-1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Troy; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ZCHEMO-8; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ZSIG-35; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Drug delivery systems
Gene therapy
Molecular cloning

(albumin fusion proteins with therapeutic proteins
for improved shelf-life)

IT CD30 (antigen)
CD40 (antigen)
Cell adhesion molecules
Cytokines
Enzymes, biological studies
Eotaxin
Erythropoietin receptors
Fas ligand

Fusion proteins (chimeric proteins)

Granulocyte-macrophage colony-stimulating factor receptors
Growth factors, animal

Interferons

Interleukin 1
Interleukin 1 receptor antagonist
Interleukin 11
Interleukin 13
Interleukin 14
Interleukin 15
Interleukin 17
Interleukin 18
Interleukin 1 α
Interleukin 1 β
Interleukin 3
Interleukin 4
Interleukin 4 receptors
Interleukin 5 receptors
Interleukin 6
Interleukin 6 receptors
Interleukin 8
Interleukin 8 receptors
Interleukin 9
Lymphotoxin
Monocyte chemoattractant protein-1
Neutrophil-activating peptide-2
Platelet-derived growth factors
RANTES (chemokine)
Stem cell factor
Synthetic gene
Tumor necrosis factor receptors
Tumor necrosis factors
Vascular endothelial growth factor receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(albumin fusion proteins with therapeutic proteins
for improved shelf-life)

IT Interleukin 10
Interleukin 12
Interleukin 2
Interleukin 5
Interleukin 7
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(albumin fusion proteins with therapeutic proteins
for improved shelf-life)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(b5; albumin fusion proteins with therapeutic
proteins for improved shelf-life)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

- (chemokine-like protein PF4-414; **albumin fusion**
proteins with therapeutic proteins for improved **shelf-life**)
- IT Growth factors, animal
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chondromodulins, -like protein; **albumin fusion**
proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(collapsins, antibodies for; **albumin fusion**
proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(exodus; **albumin fusion** proteins with therapeutic
proteins for improved **shelf-life**)
- IT Signal peptides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for improved secretion in yeast or mammalian cells; **albumin fusion**
proteins with therapeutic proteins for improved
shelf-life)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fractalkines; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
- IT Agglutinins and Lectins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(galectin-4; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gene Patched-2; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
- IT Vascular endothelial growth factor receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gene flt 1; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
- IT Vascular endothelial growth factor receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gene flt 4; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gene patched; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(glycodelin-A; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

- (granulocyte chemotactic protein-2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gro- α ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gro- β ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gro- γ ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(growth-related oncogene- α ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(growth-related oncogene- β ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(growth-related oncogene- γ ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Cytokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(interferon-inducible IP-10; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Interleukin receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(interleukin 10 receptors; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Interleukin receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(interleukin 11; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Interleukin receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(interleukin 12; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Interleukin receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(interleukin 13; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Interleukin receptors

- RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (interleukin 15; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Interleukin receptors
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (interleukin 17; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Interleukin receptors
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (interleukin 9; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (interleukin C; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (interleukin-1 accessory; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (interleukin-2 receptor associated p43; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Lymphokines
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (lymphotactins; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (macrophage **inflammatory** protein 3 α ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (macrophage **inflammatory** protein 3 β ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (macrophage **inflammatory** protein 3 γ ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Animal cell
 (mammalian, **recombinant** expression host; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Antitumor agents
 (melanoma; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

- (monocyte chemoattractant protein 3; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monocyte chemoattractant protein-1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monocyte chemoattractant protein-2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monocyte chemoattractant protein-4; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(neurotactin; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Growth factors, animal
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(osteogenic protein 2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Tumor necrosis factor receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(p75; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Plasmid vectors
(pC4:HSA, for mammalian cell expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Plasmid vectors
(pPPC0005, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Plasmid vectors
(pScCHSa, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Plasmid vectors
(pScNHSA, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Placental hormones
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(placenta-derived mitogenic factors; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Saccharomyces cerevisiae
Yeast
(recombinant expression host; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

- IT **Albumins, biological studies**
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (serum; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Genetic element
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (signal sequence, for improved secretion in yeast or mammalian cells;
 albumin fusion proteins with therapeutic proteins for improved **shelf-life**)
- IT Antibodies
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (single chain; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (stem cell inhibitory factor; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Growth factors, animal
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (stroma-derived growth factor 1 α and 1 β ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (therapeutic; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Interleukin 1 receptors
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (type 3; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Interleukin 1 receptors
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (type II; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT **Interferons**
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (α ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokine receptors
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (β chemokine receptor CCR5; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokine receptors
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (β chemokine receptor CCR7; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Transforming growth factors
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

- (β 1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Transforming growth factors
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
- (β 2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokines
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
- (β 9; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Thrombomodulin
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
- (β ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT 78990-62-2P, Calpain
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
- (10a and 10b and 10c; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT 50-56-6P, Oxytocin, biological studies 9002-62-4P, Prolactin, biological studies 9002-67-9P, Luteinizing hormone 9002-68-0P, FSH 9002-72-6P, Growth hormone 9004-10-8P, Insulin, biological studies 9014-42-0P, Thrombopoietin 11000-17-2P, Vasopressin 11096-26-7P, Erythropoietin 33507-63-0P, Substance P 67763-96-6P, Insulin-like growth factor 1 83869-56-1P, GM-CSF 106096-92-8P, Acidic fibroblast growth factor 106096-93-9P, Basic fibroblast growth factor 122191-40-6P, ICE proteinase 123584-45-2P, Fibroblast growth factor 4 129653-64-1P, Fibroblast growth factor 5 130939-41-2P, Fibroblast growth factor 6 130939-66-1P, Neurotrophin 3 140208-23-7P, Plasminogen activator inhibitor-1 141760-45-4P, Furin 142243-03-6P, Plasminogen activator inhibitor-2 143011-72-7P, G-CSF 143375-33-1P, Neurotrophin 4 148348-14-5P, Fibroblast growth factor 3 151185-16-9P, Fibroblast growth factor 9 157857-21-1P, Maspin 164003-41-2P, Fibroblast growth factor 8 185915-22-4P, Fibroblast growth factor 13 187888-07-9P, Endostatin 193363-12-1P, Vascular endothelial growth factor D 203874-76-4P, Fibroblast growth factor 12 204719-95-9P, Fibroblast growth factor 16 214210-47-6P, Neuropilin 1 219563-02-7P, Vascular endothelial growth factor E 227018-38-4P, Neuropilin 2 271597-10-5P, Growth/differentiation factor 1 322637-18-3P, Fibroblast growth factor 18 331718-56-0P, Resistin 332350-92-2P, Bone morphogenetic protein receptor kinase 3
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
- (**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT 144114-21-6, Retropepsin
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT 127464-60-2P, Vascular endothelial growth factor
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
- (isoforms; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT 127361-02-8DP, **Albumin** (human blood serum clone HSA-II/HSA-I-A protein moiety reduced), full-length or subfragment **fusion** products
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
- (nucleotide sequence; **albumin fusion** proteins with

therapeutic proteins for improved **shelf-life**)

IT 155945-98-5, PN: US5962255 SEQID: 59 unclaimed DNA 156163-00-7
 167728-69-0 167728-70-3 167728-71-4 167728-72-5 167728-73-6
 167731-70-6 167731-74-0, PN: US5962255 SEQID: 56 unclaimed DNA
 167731-75-1, PN: US5962255 SEQID: 57 unclaimed DNA 167731-76-2, PN:
 US5962255 SEQID: 58 unclaimed DNA 167731-77-3, PN: US5962255 SEQID: 60
 unclaimed DNA 167731-78-4, PN: US5962255 SEQID: 61 unclaimed DNA
 167731-79-5 167731-80-8 167731-81-9 167732-10-7 167732-11-8, PN:
 US5962255 SEQID: 551 unclaimed DNA 167732-12-9 167732-13-0
 167732-14-1, PN: US5962255 SEQID: 554 unclaimed DNA 167732-15-2, PN:
 US5962255 SEQID: 555 unclaimed DNA 167732-16-3 167732-17-4
 167732-18-5 167732-19-6, PN: US5962255 SEQID: 98 unclaimed DNA
 167732-20-9, PN: US5962255 SEQID: 572 unclaimed DNA 167732-21-0
 167732-22-1, PN: US5962255 SEQID: 574 unclaimed DNA 195164-37-5
 217893-77-1, GenBank A63614 217893-78-2, GenBank A63615 217893-79-3,
 GenBank A63616 217893-80-6, GenBank A63617 217893-81-7, GenBank A63618
 217893-82-8, GenBank A63619 217893-83-9, GenBank A63620 217893-84-0,
 GenBank A63621 217893-85-1, GenBank A63622 217893-86-2, GenBank A63624
 217893-89-5, GenBank A63627 217893-90-8, GenBank A63628 217893-91-9,
 GenBank A63629 217893-92-0, GenBank A63630 244008-03-5, PN: WO9947540
 SEQID: 3 unclaimed DNA 367319-52-6 367319-53-7 367319-54-8
 367319-55-9 367319-56-0 367319-57-1 367319-58-2 367319-59-3
 367319-60-6 367319-61-7 367319-62-8 367319-63-9 367319-64-0
 367319-65-1 367319-66-2 370965-07-4 370965-08-5
 RL: PRP (Properties)
 (unclaimed nucleotide sequence; **albumin fusion**
 proteins with therapeutic proteins for improved **shelf-life**)

IT 122024-47-9 131748-18-0 244008-06-8, PN: WO9947540 SEQID: 4 unclaimed
 DNA 244008-07-9, PN: WO9947540 SEQID: 5 unclaimed DNA 244008-08-0, PN:
 WO9947540 SEQID: 6 unclaimed DNA 244008-09-1, PN: WO9947540 SEQID: 7
 unclaimed DNA 244008-12-6, 8: PN: WO0183510 SEQID: 8 unclaimed DNA
 244008-13-7, PN: WO9947540 SEQID: 9 unclaimed DNA 367273-46-9
 367273-47-0 367273-48-1 371149-71-2
 RL: PRP (Properties)
 (unclaimed sequence; **albumin fusion** proteins with
 therapeutic proteins for improved **shelf-life**)

IT 102510-92-9P, Inhibin A
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic
 use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (α - and β -subunits; **albumin fusion**
 proteins with therapeutic proteins for improved **shelf-life**)

IT 9061-61-4P, Nerve growth factor
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic
 use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (β ; **albumin fusion** proteins with therapeutic
 proteins for improved **shelf-life**)

L66 ANSWER 8 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2001:781078 HCAPLUS
 DN 135:348850
 ED Entered STN: 26 Oct 2001
 TI **Albumin fusion** proteins with therapeutic proteins for
 improved **shelf-life**
 IN Rosen, Craig A.; Haseltine, William A.
 PA Human Genome Sciences, Inc., USA
 SO PCT Int. Appl., 374 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM C12N
 CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 3, 15

FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001079443	A2	20011025	WO 2001-US11924	20010412
	WO 2001079443	A3	20020221		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	AU 2001059063	A5	20011030	AU 2001-59063	20010412
	EP 1274719	A2	20030115	EP 2001-932546	20010412
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
	US 2003125247	A1	20030703	US 2001-833041	20010412
	US 2003171267	A1	20030911	US 2001-833117	20010412
	JP 2003530846	T2	20031021	JP 2001-577427	20010412
	US 2003199043	A1	20031023	US 2001-832501	20010412
	US 2003219875	A1	20031127	US 2001-833118	20010412
	US 2004010134	A1	20040115	US 2001-833245	20010412
PRAI	US 2000-229358P	P	20000412		
	US 2000-199384P	P	20000425		
	US 2000-256931P	P	20001221		
	WO 2001-US11924	W	20010412		
AB	The present invention encompasses fusion proteins of albumin with various therapeutic proteins. Therapeutic proteins may be stabilized to extend the shelf-life , and/or to retain the therapeutic protein's activity for extended periods of time in solution, <i>in vitro</i> and/or <i>in vivo</i> , by genetically or chemical fusing or conjugating the therapeutic protein to albumin or a fragment or variant of albumin . Use of albumin fusion proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the albumin fusion proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the albumin fusion proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired therapeutic protein may be inserted for expression of the albumin fusion proteins in yeast (pPPC0005) and mammalian cells (pC4:HSA). Yeast-derived signal sequences from <i>Saccharomyces cerevisiae</i> invertase SUC2 gene, or the stanniocalcin or native human serum albumin signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the fusion product of human growth hormone with residues 1-387 of human serum albumin retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37°, whereas recombinant human growth hormone used as control lost its biol. activity in the first week. Although the potency of the albumin fusion proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. stability results in much higher biol. activity in the longer term <i>in vitro</i> assay or <i>in vivo</i> assays. Addnl., the present invention encompasses pharmaceutical compns. comprising albumin fusion proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using albumin fusion proteins of the invention.				
ST	albumin fusion therapeutic protein shelflife				

- IT Bone morphogenetic proteins
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Bone morphogenetic proteins
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (7; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Transport proteins
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (ABC1 (ATP-binding cassette-containing 1); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (ADM1 (anti-dorsalizing morphogenetic protein-1); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (Agouti signal; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (BPI (bactericidal/permeability-increasing), 21; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Transcription factors
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (BRCA1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Transcription factors
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (BRCA2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (Del-1 (developmentally regulated endothelial locus-1); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (EMAP II (endothelial monocyte activating polypeptide II); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Troponins
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (I; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Toxins
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(ML-I (mistletoe lectin I); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MTP (microsomal transfer protein); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NIF (neutrophil inhibitory factor); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(T1/ST2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Glycoproteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TNF-BP (tumor necrosis factor-binding protein); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TRAIL (tumor necrosis factor-related apoptosis-inducing ligand); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Drug delivery systems
Gene therapy
Molecular cloning
(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Arrestins
CD4 (antigen)
CTLA-4 (antigen)
Calreticulin
Cell adhesion molecules
Ciliary **neurotrophic** factor
Cytokines
Decorins
Enzymes, biological studies
Fusion proteins (chimeric proteins)
Gelsolin
Growth factors, animal
Heat-shock proteins
Interferons
Interleukin 1
Interleukin 1 receptor antagonist
Interleukin 10
Interleukin 11
Interleukin 12
Interleukin 18
Interleukin 4
Interleukin 4 receptors
Interleukin 8
LFA-3 (antigen)
Lactoferrins
Leukemia inhibitory factor
Myelin basic protein

- Platelet-derived growth factors
 Pleiotrophins
 Stem cell factor
 Synthetic gene
 Tumor necrosis factor receptors
 Tumor necrosis factor receptors
 Tumor necrosis factors
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (**albumin fusion** proteins with therapeutic proteins
 for improved **shelf-life**)
- IT **Neurotrophic factors**
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (**brain-derived; albumin fusion**
 proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (**chemokine-binding; albumin fusion** proteins with
 therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (**corticotropin-releasing factor-binding; albumin fusion**
 proteins with therapeutic proteins for improved
shelf-life)
- IT Toxins
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (**diphtheria, fusion** protein with interleukin 2;
albumin fusion proteins with therapeutic proteins for
 improved **shelf-life**)
- IT Toxins
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (**exotoxins, Pseudomonas, fusion** protein with acidic
 fibroblast growth factor; **albumin fusion** proteins
 with therapeutic proteins for improved **shelf-life**)
- IT Signal peptides
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (for improved secretion in yeast or mammalian cells; **albumin fusion**
 proteins with therapeutic proteins for improved
shelf-life)
- IT Interleukin 3
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (**fusion** protein with G-CSF; **albumin fusion**
 proteins with therapeutic proteins for improved **shelf-life**)
- IT Interleukin 6
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (**fusion** proteins with diphtheria toxin or Pseudomonas
 exotoxin; **albumin fusion** proteins with therapeutic
 proteins for improved **shelf-life**)
- IT Proteins, specific or class
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (**gene patched; albumin fusion** proteins with
 therapeutic proteins for improved **shelf-life**)

- IT **Neurotrophic factors**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(glial-derived; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT **Interferons**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**interferon** α ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**interferon**-induced, 10; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Animal cell
(mammalian, **recombinant** expression host; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(noggins; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Plasmid vectors
(pC4:HSA, for mammalian cell expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Plasmid vectors
(pPPC0005, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Plasmid vectors
(pScCHSa, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Plasmid vectors
(pScNHSA, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Hemopoietins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(progenipoietin; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Hemopoietins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(promegapoietin; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Saccharomyces cerevisiae
Yeast
(**recombinant** expression host; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Antigens
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(retinal S-; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT **Albumins, biological studies**

- RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(serum; **albumin fusion** proteins with therapeutic
proteins for improved **shelf-life**)
- IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(signal sequence, for improved secretion in yeast or mammalian cells;
albumin fusion proteins with therapeutic proteins for
improved **shelf-life**)
- IT Antibodies
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(single chain; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
- IT Hedgehog protein
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(sonic; **albumin fusion** proteins with therapeutic
proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tie-2; **albumin fusion** proteins with therapeutic
proteins for improved **shelf-life**)
- IT Complement receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(type 1; **albumin fusion** proteins with therapeutic
proteins for improved **shelf-life**)
- IT Collagens, biological studies
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(type II; **albumin fusion** proteins with therapeutic
proteins for improved **shelf-life**)
- IT **Interferons**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(τ ; **albumin fusion** proteins with therapeutic
proteins for improved **shelf-life**)
- IT **Interferons**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(α ; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
- IT Transforming growth factors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β_1 -; **albumin fusion** proteins with therapeutic
proteins for improved **shelf-life**)
- IT Transforming growth factors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β_2 -; **albumin fusion** proteins with therapeutic
proteins for improved **shelf-life**)
- IT Transforming growth factors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

- (β 3-; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT **Interferons**
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (γ ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT 139691-92-2P, Serine proteinase inhibitor
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT 9001-91-6DP, Lys-plasminogen, de-(1-76) derivs.
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (Lys-plasminogen; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT 9001-42-7P, α -Glucosidase 9002-01-1P, Streptokinase 9002-12-4P,
 Urate oxidase 9002-61-3P, Chorionic gonadotropin 9002-67-9P,
 Luteinizing hormone 9002-68-0P, FSH 9002-69-1P, Relaxin 9002-72-6P,
 Growth hormone 9003-98-9P, DNase 9004-10-8P, Insulin, biological
 studies 9007-92-5P, Glucagon, biological studies 9014-42-0P,
 Thrombopoietin 9015-68-3P, Asparaginase 9025-35-8P,
 α -Galactosidase 9026-93-1P, Adenosine deaminase 9035-55-6P,
 Adiposin 9039-53-6P, Urokinase 9040-61-3P, Staphylokinase
 9054-89-1DP, Superoxide dismutase, **fusion** protein with botulin
 9061-61-4P, Nerve growth factor 9073-56-7P, α -L-Iduronidase
 9088-41-9P, Kunitz proteinase inhibitor 11096-26-7P, Erythropoietin
 37228-64-1P, β -Glucocerebrosidase 42616-25-1P, Methioninase
 55354-43-3P, Arylsulfatase B 62229-50-9P, Epidermal growth factor
 67763-96-6P, Insulin-like growth factor 1 76901-00-3P, Platelet
 activating factor acetylhydrolase 82707-54-8P, Neprilysin 83652-28-2P,
 Calcitonin gene-related peptide 83869-56-1P, GM-CSF 86090-08-6P,
 Angiostatin 99149-95-8P, Saruplase 104625-48-1P, Activin A
 105844-41-5P, Plasminogen activator inhibitor 106096-92-8DP, Acidic
 fibroblast growth factor, **fusion** protein with Pseudomonas
 exotoxin 106096-92-8P 106096-93-9P, Fibroblast growth factor 2
 107231-12-9DP, Botulin, **fusion** protein with superoxide dismutase
 116036-70-5P, Fibrolase 130939-66-1P, Neurotrophin 3 139639-23-9P,
 Tissue-type plasminogen activator 143011-72-7P, G-CSF 145137-38-8P,
 Desmoteplase 153858-68-5P, Contortrostatin 157857-21-1P, Maspin
 163658-39-7P, Prosaptide 169494-85-3P, Leptin 186270-49-5P,
 Angiopoietin 1 194368-66-6P, Angiopoietin 2 194554-71-7P, Tissue
 factor pathway inhibitor 195009-21-3P, Glial growth factor 2
 196488-72-9P, Ranpirnase 197980-93-1P, Pigment epithelium-derived factor
 205944-50-9P, Osteoprotegerin 244019-30-5P, Vascular endothelial growth
 factor 1 320336-96-7P, Kistrin 362605-29-6P, Keratinocyte growth
 factor 1
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT 9000-95-7P, Apyrase
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (ecto-; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT 9002-79-3P, MSH
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (**fusion** products with diphtheria toxin; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 127361-02-8DP, **Albumin** (human blood serum clone HSA-II/HSA-I-A protein moiety reduced), full-length or subfragment **fusion** products
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (nucleotide sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 131748-18-0 156163-00-7 217893-77-1, GenBank A63614 217893-78-2,
 GenBank A63615 217893-79-3, GenBank A63616 217893-80-6, GenBank A63617
 217893-81-7, GenBank A63618 217893-82-8, GenBank A63619 217893-83-9,
 GenBank A63620 217893-84-0, GenBank A63621 217893-85-1, GenBank A63622
 217893-86-2, GenBank A63624 217893-89-5, GenBank A63627 217893-90-8,
 GenBank A63628 217893-91-9, GenBank A63629 217893-92-0, GenBank A63630
 367319-52-6 367319-53-7 367319-54-8 367319-55-9 367319-56-0
 367319-58-2 367319-59-3 367319-60-6 367319-61-7 367319-62-8
 367319-63-9 367319-64-0 367319-65-1 367319-66-2
 RL: PRP (Properties)
 (unclaimed nucleotide sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 229477-44-5 244008-03-5, PN: WO9947540 SEQID: 3 unclaimed DNA
 244008-06-8, PN: WO9947540 SEQID: 4 unclaimed DNA 244008-07-9, PN:
 WO9947540 SEQID: 5 unclaimed DNA 244008-08-0, PN: WO9947540 SEQID: 6
 unclaimed DNA 244008-09-1, PN: WO9947540 SEQID: 7 unclaimed DNA
 244008-12-6, 8: PN: WO0183510 SEQID: 8 unclaimed DNA 244008-13-7, PN:
 WO9947540 SEQID: 9 unclaimed DNA 244008-14-8, PN: WO9947540 SEQID: 10
 unclaimed DNA 367273-46-9 367273-47-0 367273-48-1 370571-84-9
 RL: PRP (Properties)
 (unclaimed sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 114949-22-3P, Activin
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (β c; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

L66 ANSWER 9 OF 29 HCPLUS COPYRIGHT 2004 ACS on STN
 AN 2001:781077 HCPLUS
 DN 135:348849
 ED Entered STN: 26 Oct 2001
 TI **Albumin fusion** proteins with therapeutic proteins for improved **shelf-life**
 IN Rosen, Craig A.; Haseltine, William A.
 PA Human Genome Sciences, Inc., USA
 SO PCT Int. Appl., 413 pp.
 CODEN: PIXXD2
 DT Patent
 IA English
 IC ICM C12N
 CC 63-3 (Pharmaceuticals)
 Section cross-reference(s): 3, 15

FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001079442	A2	20011025	WO 2001-US11850	20010412
	WO 2001079442	A3	20020606		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,			

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BE,
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 AU 2001064563 A5 20011030 AU 2001-64563 20010412
 EP 1276849 A2 20030122 EP 2001-938994 20010412
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 US 2003125247 A1 20030703 US 2001-833041 20010412
 US 2003171267 A1 20030911 US 2001-833117 20010412
 US 2003199043 A1 20031023 US 2001-832501 20010412
 JP 2003531590 T2 20031028 JP 2001-577426 20010412
 US 2003219875 A1 20031127 US 2001-833118 20010412
 US 2004010134 A1 20040115 US 2001-833245 20010412
 PRAI US 2000-229358P P 20000412
 US 2000-199384P P 20000425
 US 2000-256931P P 20001221
 WO 2001-US11850 W 20010412

AB The present invention encompasses **fusion** proteins of **albumin** with various therapeutic proteins, and in particular various antibodies. Therapeutic proteins may be stabilized to extend the **shelf-life**, and/or to retain the therapeutic protein's activity for extended periods of time in solution, in vitro and/or in vivo, by genetically or chemical **fusing** or conjugating the therapeutic protein to **albumin** or a fragment or variant of **albumin**.
 Use of **albumin fusion** proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the **albumin fusion** proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the **albumin fusion** proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired therapeutic protein may be inserted for expression of the **albumin fusion** proteins in yeast (pPPC0005) and mammalian cells (pC4:HSA). Yeast-derived signal sequences from *Saccharomyces cerevisiae* invertase SUC2 gene, or the stanniocalcin or native human serum **albumin** signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the **fusion** product of human growth hormone with residues 1-387 of human serum **albumin** retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37°, whereas **recombinant** human growth hormone used as control lost its biol. activity in the first week. Although the potency of the **albumin fusion** proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. stability results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical comps. comprising **albumin fusion** proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using **albumin fusion** proteins of the invention.

ST **albumin fusion therapeutic protein shelflife**
 IT Antigens
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (17-1A, antibodies to; **albumin fusion** proteins with
 therapeutic proteins for improved **shelf-life**)
 IT Proteins, specific or class
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (B7.2, antibodies to; **albumin fusion** proteins with
 therapeutic proteins for improved **shelf-life**)
 IT Proteins, specific or class
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (CA125, antibodies to; **albumin fusion** proteins with
 therapeutic proteins for improved **shelf-life**)

- IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD147, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD33, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD48, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD52, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD6, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (E, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (HLA-DR, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (HMI.24, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ICAM-1 (intercellular adhesion mol. 1), antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Immunoglobulin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (IgG type I, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Selectins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (L-, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (LPAM-1 (lymphocyte Peyer's patch high endothelial venule adhesion mol. 1), antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Blood-group substances
RL: BSU (Biological study, unclassified); BIOL (Biological study) (Lex, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Blood-group substances
RL: BSU (Biological study, unclassified); BIOL (Biological study) (Ley, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (M, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
- IT Histocompatibility antigens

- RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MHC (major histocompatibility complex), class I, antibodies to;
albumin fusion proteins with therapeutic proteins for
improved **shelf-life**)
- IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MHC (major histocompatibility complex), class II, antibodies to;
albumin fusion proteins with therapeutic proteins for
improved **shelf-life**)
- IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NogoA, antibodies to; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Nsf2, antibodies to; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
- IT Glycoproteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(P170, antibodies to; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
- IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(SC-1, antibodies to; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(SF-25, antibodies to; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
- IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(SSEA-1 (stage-specific embryonic antigen 1), antibodies to;
albumin fusion proteins with therapeutic proteins for
improved **shelf-life**)
- IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TAG-72 (tumor-associated glycoprotein 72), antibodies to; **albumin**
fusion proteins with therapeutic proteins for improved
shelf-life)
- IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(VCAM-1, antibodies to; **albumin fusion** proteins
with therapeutic proteins for improved **shelf-life**)
- IT Drug delivery systems
Gene therapy
Molecular cloning
 (**albumin fusion** proteins with therapeutic proteins
 for improved **shelf-life**)
- IT Antibodies
Cell adhesion molecules
Cytokines
Enzymes, biological studies
 Fusion proteins (chimeric proteins)
Growth factors, animal
Immunoglobulins
 Interferons
Synthetic gene
Tumor necrosis factor receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic
use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (**albumin fusion** proteins with therapeutic proteins
 for improved **shelf-life**)
- IT Angiogenic factors

CD14 (antigen)
CD2 (antigen)
CD20 (antigen)
CD22 (antigen)
CD3 (antigen)
CD30 (antigen)
CD38 (antigen)
CD4 (antigen)
CD40 (antigen)
CD44 (antigen)
CD45 (antigen)
CD5 (antigen)
CD8 (antigen)
CD80 (antigen)
CD80 (antigen)
CTLA-4 (antigen)
Carcinoembryonic antigen
Epidermal growth factor receptors
Fas antigen
Integrins
Interleukin 4 receptors
Interleukin 5
LFA-1 (antigen)
Mucins
TCR (T cell receptors)
Transferrin receptors
neu (receptor)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibodies to; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
IT Mucins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(episialins, antibodies to; **albumin fusion** proteins
with therapeutic proteins for improved **shelf-life**)
IT Signal peptides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(for improved secretion in yeast or mammalian cells; **albumin fusion**
proteins with therapeutic proteins for improved
shelf-life)
IT Glycoproteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gD, antibodies to; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
IT Envelope proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gp120env, antibodies to; **albumin fusion** proteins
with therapeutic proteins for improved **shelf-life**)
IT Glycoproteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gpII, antibodies to; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
IT Animal cell
(mammalian, **recombinant** expression host; **albumin fusion**
proteins with therapeutic proteins for improved
shelf-life)
IT Agglutinins and Lectins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mannan-binding, antibodies to; **albumin fusion**
proteins with therapeutic proteins for improved **shelf-life**)
IT Antibodies
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic

- use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
- IT Plasmid vectors
(pC4:HSA, for mammalian cell expression; **albumin fusion**
proteins with therapeutic proteins for improved **shelf-life**)
- IT Plasmid vectors
(pPPC0005, for yeast expression; **albumin fusion**
proteins with therapeutic proteins for improved **shelf-life**)
- IT Plasmid vectors
(pScCHSa, for yeast expression; **albumin fusion**
proteins with therapeutic proteins for improved **shelf-life**)
- IT Plasmid vectors
(pScNHSA, for yeast expression; **albumin fusion**
proteins with therapeutic proteins for improved **shelf-life**)
- IT Interleukin 6 receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptor-associated glycoprotein gp130, antibodies to; **albumin fusion**
proteins with therapeutic proteins for improved **shelf-life**)
- IT Saccharomyces cerevisiae
Yeast
(**recombinant** expression host; **albumin fusion**
proteins with therapeutic proteins for improved **shelf-life**)
- IT **Albumins, biological studies**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(serum; **albumin fusion** proteins with therapeutic
proteins for improved **shelf-life**)
- IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(signal sequence, for improved secretion in yeast or mammalian cells;
albumin fusion proteins with therapeutic proteins for
improved **shelf-life**)
- IT Antibodies
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(single chain; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
- IT Venoms
(snake, antibodies to; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic; **albumin fusion** proteins with
therapeutic proteins for improved **shelf-life**)
- IT Globulins, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(thymocyte, antibodies to; **albumin fusion** proteins
with therapeutic proteins for improved **shelf-life**)
- IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tumor-associated, antibodies to; **albumin fusion**
proteins with therapeutic proteins for improved **shelf-life**)
- IT Interleukin 2 receptors

- RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (α -chain, antibodies to; **albumin fusion**
 proteins with therapeutic proteins for improved **shelf-life**)
- IT Interferons
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (α ; **albumin fusion** proteins with
 therapeutic proteins for improved **shelf-life**)
- IT Integrins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (α IIb β 3, antibodies to; **albumin fusion**
 proteins with therapeutic proteins for improved **shelf-life**)
- IT Vitronectin receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (α v β 3, antibodies to; **albumin fusion**
 proteins with therapeutic proteins for improved **shelf-life**)
- IT Integrins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (α 4 β 1, antibodies to; **albumin fusion**
 proteins with therapeutic proteins for improved **shelf-life**)
- IT Chemokine receptors.
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (β chemokine receptor CCR5, antibodies to; **albumin fusion**
 proteins with therapeutic proteins for improved **shelf-life**)
- IT Integrins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (β 2, antibodies to; **albumin fusion** proteins
 with therapeutic proteins for improved **shelf-life**)
- IT 9002-67-9P, Luteinizing hormone 9002-68-0P, FSH 9002-72-6P, Growth
 hormone 9004-10-8P, Insulin, biological studies 11096-26-7P,
 Erythropoietin 67763-96-6P, Insulin-like growth factor 1 83869-56-1P,
 GM-CSF 143011-72-7P, G-CSF
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (**albumin fusion** proteins with therapeutic proteins
 for improved **shelf-life**)
- IT 156586-89-9
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (**albumin fusion** proteins with therapeutic proteins
 for improved **shelf-life**)
- IT 11016-39-0, Properdin 19600-01-2, Ganglioside GM2 20830-75-5, Digoxin
 99085-47-9, CD55 antigen
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (antibodies to; **albumin fusion** proteins with
 therapeutic proteins for improved **shelf-life**)
- IT 127361-02-8DP, **Albumin** (human blood serum clone HSA-II/HSA-I-A
 protein moiety reduced), full-length or subfragment **fusion**
 products
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (nucleotide sequence; **albumin fusion** proteins with
 therapeutic proteins for improved **shelf-life**)
- IT 155945-98-5, PN: US5962255 SEQID: 59 unclaimed DNA 156163-00-7
 167728-69-0 167728-70-3 167728-71-4 167728-72-5 167728-73-6
 167731-70-6 167731-74-0, PN: US5962255 SEQID: 56 unclaimed DNA
 167731-75-1, PN: US5962255 SEQID: 57 unclaimed DNA 167731-76-2, PN:
 US5962255 SEQID: 58 unclaimed DNA 167731-77-3, PN: US5962255 SEQID: 60
 unclaimed DNA 167731-78-4, PN: US5962255 SEQID: 61 unclaimed DNA

167731-79-5 167731-80-8 167731-81-9 167732-10-7 167732-11-8, PN:
 US5962255 SEQID: 551 unclaimed DNA 167732-12-9 167732-13-0
 167732-14-1, PN: US5962255 SEQID: 554 unclaimed DNA 167732-15-2, PN:
 US5962255 SEQID: 555 unclaimed DNA 167732-16-3 167732-17-4
 167732-18-5 167732-19-6, PN: US5962255 SEQID: 98 unclaimed DNA
 167732-20-9, PN: US5962255 SEQID: 572 unclaimed DNA 167732-21-0
 167732-22-1, PN: US5962255 SEQID: 574 unclaimed DNA 195164-37-5
 217893-77-1, GenBank A63614 217893-78-2, GenBank A63615 217893-79-3,
 GenBank A63616 217893-80-6, GenBank A63617 217893-81-7, GenBank A63618
 217893-82-8, GenBank A63619 217893-83-9, GenBank A63620 217893-84-0,
 GenBank A63621 217893-85-1, GenBank A63622 217893-86-2, GenBank A63624
 217893-89-5, GenBank A63627 217893-90-8, GenBank A63628 217893-91-9,
 GenBank A63629 217893-92-0, GenBank A63630 367319-52-6 367319-53-7
 367319-54-8 367319-55-9 367319-56-0 367319-57-1 367319-58-2
 367319-59-3 367319-60-6 367319-61-7 367319-62-8 367319-63-9
 367319-64-0 367319-65-1 367319-66-2

RL: PRP (Properties)

(unclaimed nucleotide sequence; **albumin fusion**
 proteins with therapeutic proteins for improved **shelf-life**)

IT 122024-47-9 131748-18-0 229477-44-5 244008-03-5, PN: WO9947540
 SEQID: 3 unclaimed DNA 244008-06-8, PN: WO9947540 SEQID: 4 unclaimed DNA
 244008-07-9, PN: WO9947540 SEQID: 5 unclaimed DNA 244008-08-0, PN:
 WO9947540 SEQID: 6 unclaimed DNA 244008-09-1, PN: WO9947540 SEQID: 7
 unclaimed DNA 244008-12-6, 8: PN: WO0183510 SEQID: 8 unclaimed DNA
 244008-13-7, PN: WO9947540 SEQID: 9 unclaimed DNA 244008-14-8, PN:
 WO9947540 SEQID: 10 unclaimed DNA 367273-46-9 367273-47-0
 367273-48-1

RL: PRP (Properties)

(unclaimed sequence; **albumin fusion** proteins with
 therapeutic proteins for improved **shelf-life**)

L66 ANSWER 10 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:780938 HCAPLUS

DN 135:322686

ED Entered STN: 26 Oct 2001

TI **Albumin fusion** proteins with therapeutic proteins for
 improved **shelf-life**

IN Rosen, Craig A.; Sadeghi, Homayoun; Prior, Christopher P.;
 Turner, Andrew John

PA Human Genome Sciences, Inc., USA; Principia Pharmaceutical
 Corporation

SO PCT Int. Appl., 328 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07K001-00

ICS A01N037-18

CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 3, 15

FAN.CNT 7

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
------------	------	------	-----------------	------

PI	WO 2001079258	A1	20011025	WO 2001-US12008	20010412
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

EP 1274720	A1	20030115	EP 2001-932549	20010412
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003125247	A1	20030703	US 2001-833041	20010412
US 2003171267	A1	20030911	US 2001-833117	20010412
JP 2003530838	T2	20031021	JP 2001-576855	20010412
US 2003199043	A1	20031023	US 2001-832501	20010412
US 2003219875	A1	20031127	US 2001-833118	20010412
US 2004010134	A1	20040115	US 2001-833245	20010412

PRAI US 2000-229358P P 20000412
 US 2000-199384P P 20000425
 US 2000-256931P P 20001221
 WO 2001-US12008 W 20010412

AB The present invention encompasses **fusion** proteins of **albumin** with various therapeutic proteins, and in particular, with interleukin 2, calcitonin, growth hormone-releasing factor, **interferon** β , parathyroid hormone, and insulin-like growth factor 1. Therapeutic proteins may be stabilized to extend the **shelf-life**, and/or to retain the therapeutic protein's activity for extended periods of time in solution, in vitro and/or in vivo, by genetically or chemical **fusing** or conjugating the therapeutic protein to **albumin** or a fragment or variant of **albumin**.
 Use of **albumin fusion** proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the **albumin fusion** proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the **albumin fusion** proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired therapeutic protein may be inserted for expression of the **albumin fusion** proteins in yeast (pPPC0005) and mammalian cells (pc4:HSA). Yeast-derived signal sequences from Saccharomyces cerevisiae invertase SUC2 gene, or the stanniocalcin or native human serum **albumin** signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the **fusion** product of human growth hormone with residues 1-387 of human serum **albumin** retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37°, whereas **recombinant** human growth hormone used as control lost its biol. activity in the first week. Although the potency of the **albumin fusion** proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. stability results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical compns. comprising **albumin fusion** proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using **albumin fusion** proteins of the invention.

ST **albumin fusion therapeutic protein shelflife**

IT Hepatitis

(C, agents for treatment of; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antitumor agents

(Kaposi's sarcoma; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antitumor agents

(acute myelogenous leukemia; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Anti-AIDS agents

Antidiabetic agents

Antirheumatic agents
Drug delivery systems
Gene therapy
Immunosuppressants
Molecular cloning
 (albumin fusion proteins with therapeutic proteins
 for improved shelf-life)

IT Cell adhesion molecules
Cytokines
Enzymes, biological studies
 Fusion proteins (chimeric proteins)
Growth factors, animal
 Interferons
Interleukin 2
Synthetic gene
Tumor necrosis factor receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (albumin fusion proteins with therapeutic proteins
 for improved shelf-life)

IT Signal peptides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (for improved secretion in yeast or mammalian cells; albumin
 fusion proteins with therapeutic proteins for improved
 shelf-life)

IT Intestine, disease
 (inflammatory, agents for treatment of; albumin
 fusion proteins with therapeutic proteins for improved
 shelf-life)

IT Kidney, neoplasm
Lung, neoplasm
Ovary, neoplasm
 (inhibitors; albumin fusion proteins with
 therapeutic proteins for improved shelf-life)

IT Antitumor agents
 (kidney; albumin fusion proteins with therapeutic
 proteins for improved shelf-life)

IT Antitumor agents
 (leukemia; albumin fusion proteins with therapeutic
 proteins for improved shelf-life)

IT Antitumor agents
 (lung; albumin fusion proteins with therapeutic
 proteins for improved shelf-life)

IT Animal cell
 (mammalian, recombinant expression host; albumin
 fusion proteins with therapeutic proteins for improved
 shelf-life)

IT Antitumor agents
 (melanoma, metastasis; albumin fusion proteins with
 therapeutic proteins for improved shelf-life)

IT Antitumor agents
 (melanoma; albumin fusion proteins with therapeutic
 proteins for improved shelf-life)

IT Antitumor agents
 (non-Hodgkin's lymphoma; albumin fusion proteins
 with therapeutic proteins for improved shelf-life)

IT Antitumor agents
 (ovary; albumin fusion proteins with therapeutic
 proteins for improved shelf-life)

IT Plasmid vectors
 (pC4:HSA, for mammalian cell expression; albumin
 fusion proteins with therapeutic proteins for improved

- shelf-life)
- IT Plasmid vectors
(pPPC0005, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT Plasmid vectors
(pScCHSa, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT Plasmid vectors
(pScNHSA, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT Saccharomyces cerevisiae
Yeast
(recombinant expression host; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT Kidney, neoplasm
(renal-cell carcinoma, metastasis, inhibitors; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT Antitumor agents
(renal-cell carcinoma, metastasis; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT **Albumins, biological studies**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(serum; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(signal sequence, for improved secretion in yeast or mammalian cells; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT Antibodies
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(single chain; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT Multiple sclerosis
(therapeutic agents; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT **Interferons**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(α ; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT **Interferons**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β ; **albumin fusion** proteins with therapeutic proteins for improved shelf-life)
- IT 9002-64-6P, Parathyroid hormone 9002-67-9P, Luteinizing hormone
9002-68-0P, FSH 9002-72-6P, Growth hormone 9004-10-8P, Insulin,
biological studies 9007-12-9P, Calcitonin 9034-39-3P, Growth

hormone-releasing factor 11096-26-7P, Erythropoietin 67763-96-6P, Insulin-like growth factor 1 83869-56-1P, GM-CSF 143011-72-7P, G-CSF
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (albumin fusion proteins with therapeutic proteins
 for improved shelf-life)

- IT 127361-02-8DP, **Albumin** (human blood serum clone HSA-II/HSA-I-A protein moiety reduced), full-length or subfragment **fusion** products
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (nucleotide sequence; albumin fusion proteins with therapeutic proteins for improved shelf-life)
- IT 156163-00-7 217893-77-1, GenBank A63614 217893-78-2, GenBank A63615
 217893-79-3, GenBank A63616 217893-80-6, GenBank A63617 217893-81-7,
 GenBank A63618 217893-82-8, GenBank A63619 217893-83-9, GenBank A63620
 217893-84-0, GenBank A63621 217893-85-1, GenBank A63622 217893-86-2,
 GenBank A63624 217893-89-5, GenBank A63627 217893-90-8, GenBank A63628
 217893-91-9, GenBank A63629 217893-92-0, GenBank A63630 244008-03-5,
 PN: WO9947540 SEQID: 3 unclaimed DNA 244008-06-8, PN: WO9947540 SEQID: 4
 unclaimed DNA 244008-07-9, PN: WO9947540 SEQID: 5 unclaimed DNA
 244008-08-0, PN: WO9947540 SEQID: 6 unclaimed DNA 244008-09-1, PN:
 WO9947540 SEQID: 7 unclaimed DNA 244008-12-6, 8: PN: WO0183510 SEQID: 8
 unclaimed DNA 244008-13-7, PN: WO9947540 SEQID: 9 unclaimed DNA
 244008-14-8, PN: WO9947540 SEQID: 10 unclaimed DNA 367319-52-6
 367319-53-7 367319-54-8 367319-55-9 367319-56-0 367319-57-1
 367319-58-2 367319-59-3 367319-60-6 367319-61-7 367319-62-8
 367319-63-9 367319-64-0 367319-65-1 367319-66-2 367319-67-3
 RL: PRP (Properties)
 (unclaimed nucleotide sequence; albumin fusion
 proteins with therapeutic proteins for improved shelf-
 life)

- IT 367510-76-7
 RL: PRP (Properties)
 (unclaimed protein sequence; albumin fusion
 proteins with therapeutic proteins for improved shelf-
 life)
- IT 131748-18-0 367273-46-9 367273-47-0 367273-48-1
 RL: PRP (Properties)
 (unclaimed sequence; albumin fusion proteins with
 therapeutic proteins for improved shelf-life)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Beth Israel Hospital Association; WO 9618412 A1 1996 HCPLUS
- (2) Lee; Pharm Dev Tech 1999, V4(2), P269 HCPLUS
- (3) Rhone-Poulenc Rorer S A; WO 9315199 A1 1993 HCPLUS
- (4) Rhone-Poulenc Rorer S A; WO 9315211 A1 1993 HCPLUS
- (5) Takahashi; Peptides 1997, V18(3), P439 HCPLUS
- (6) Yeh; Prc Nat Acad Sci USA 1992, V69, P1904

L66 ANSWER 11 OF 29 HCPLUS COPYRIGHT 2004 ACS on STN

AN 2001:763025 HCPLUS

DN 135:335111

ED Entered STN: 19 Oct 2001

TI Albumin fusion proteins with therapeutic proteins for improved shelf-life

IN Rosen, Craig A.; Haseltine, William A.

PA Human Genome Sciences, Inc., USA

SO PCT Int. Appl., 2102 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07H021-04

CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 3, 15

FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001077137	A1	20011018	WO 2001-US11988	20010412
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1276756	A1	20030122	EP 2001-944114	20010412
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003125247	A1	20030703	US 2001-833041	20010412
	US 2003171267	A1	20030911	US 2001-833117	20010412
	US 2003199043	A1	20031023	US 2001-832501	20010412
	US 2003219875	A1	20031127	US 2001-833118	20010412
	US 2004010134	A1	20040115	US 2001-833245	20010412
PRAI	US 2000-229358P	P	20000412		
	US 2000-199384P	P	20000425		
	US 2000-256931P	P	20001221		
	WO 2001-US11988	W	20010412		

AB The present invention encompasses fusion proteins of albumin with various therapeutic proteins. Therapeutic proteins may be stabilized to extend the shelf-life, and/or to retain the therapeutic protein's activity for extended periods of time in solution, in vitro and/or in vivo, by genetically or chemical fusing or conjugating the therapeutic protein to albumin or a fragment or variant of albumin. Use of albumin fusion proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the albumin fusion proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the albumin fusion proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired therapeutic protein may be inserted for expression of the albumin fusion proteins in yeast (ppPC0005) and mammalian cells (pC4:HSA). Yeast-derived signal sequences from *Saccharomyces cerevisiae* invertase SUC2 gene, or the stanniocalcin or native human serum albumin signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the fusion product of human growth hormone with residues 1-387 of human serum albumin retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37°, whereas recombinant human growth hormone used as control lost its biol. activity in the first week. Although the potency of the albumin fusion proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. stability results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical compns. comprising albumin fusion proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using albumin fusion proteins of the invention.

ST albumin fusion therapeutic protein shelflife

IT Drug delivery systems

Gene therapy

Molecular cloning

(albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Cell adhesion molecules

Cytokines
Enzymes, biological studies
Fusion proteins (chimeric proteins)
Growth factors, animal
Interferons
Synthetic gene
Tumor necrosis factor receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Signal peptides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for improved secretion in yeast or mammalian cells; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Animal cell
(mammalian, recombinant expression host; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Plasmid vectors
(pC4:HSA, for mammalian cell expression; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Plasmid vectors
(pPPC0005, for yeast expression; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Plasmid vectors
(pScCHSA, for yeast expression; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Plasmid vectors
(pScNHSA, for yeast expression; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Saccharomyces cerevisiae
Yeast
(recombinant expression host; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Albumins, biological studies
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(serum; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(signal sequence, for improved secretion in yeast or mammalian cells; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Antibodies
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(single chain; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Interferons
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(α ; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT 9002-67-9P, Luteinizing hormone 9002-68-0P, FSH 9002-72-6P, Growth hormone 9004-10-8P, Insulin, biological studies 11096-26-7P,

Erythropoietin 67763-96-6P, Insulin-like growth factor 1 83869-56-1P,
 GM-CSF 143011-72-7P, G-CSF
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic
 use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (albumin fusion proteins with therapeutic proteins for improved
 shelf-life)

IT 127361-02-8DP, Albumin (human blood serum clone HSA-II/HSA-I-A protein
 moiety reduced), full-length or subfragment fusion products
 RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic
 use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (nucleotide sequence; albumin fusion proteins with therapeutic proteins
 for improved shelf-life)

IT 155945-98-5, PN: US5962255 SEQID: 59 unclaimed DNA 156163-00-7
 167728-69-0 167728-70-3 167728-71-4 167728-72-5 167728-73-6
 167731-70-6 167731-74-0, PN: US5962255 SEQID: 56 unclaimed DNA
 167731-75-1, PN: US5962255 SEQID: 57 unclaimed DNA 167731-76-2, PN:
 US5962255 SEQID: 58 unclaimed DNA 167731-77-3, PN: US5962255 SEQID: 60
 unclaimed DNA 167731-78-4, PN: US5962255 SEQID: 61 unclaimed DNA
 167731-79-5 167731-80-8 167731-81-9 167732-10-7 167732-11-8, PN:
 US5962255 SEQID: 551 unclaimed DNA 167732-12-9 167732-13-0
 167732-14-1, PN: US5962255 SEQID: 554 unclaimed DNA 167732-15-2, PN:
 US5962255 SEQID: 555 unclaimed DNA 167732-16-3 167732-17-4
 167732-18-5 167732-19-6, PN: US5962255 SEQID: 98 unclaimed DNA
 167732-20-9, PN: US5962255 SEQID: 572 unclaimed DNA 167732-21-0
 167732-22-1, PN: US5962255 SEQID: 574 unclaimed DNA 195164-37-5
 217893-77-1, GenBank A63614 217893-78-2, GenBank A63615 217893-79-3,
 GenBank A63616 217893-80-6, GenBank A63617 217893-81-7, GenBank A63618
 217893-82-8, GenBank A63619 217893-83-9, GenBank A63620 217893-84-0,
 GenBank A63621 217893-86-2, GenBank A63624 217893-89-5, GenBank A63627
 217893-90-8, GenBank A63628 217893-91-9, GenBank A63629 217893-92-0,
 GenBank A63630 367319-52-6 367319-53-7 367319-54-8 367319-55-9
 367319-56-0 367319-57-1 367319-58-2 367319-59-3 367319-60-6
 367319-61-7 367319-62-8 367319-64-0 367319-65-1 367319-66-2
 367985-08-8
 RL: PRP (Properties)
 (unclaimed nucleotide sequence; albumin fusion proteins with
 therapeutic proteins for improved shelf-life)

IT 135688-15-2, Complement C1q (human clone pC1qA8.0E A-chain precursor
 protein moiety reduced) 151187-86-9 160405-14-1 160405-30-1
 161477-27-6 180191-50-8 208473-02-3 208668-41-1 208885-10-3,
 Gremlin (human) 209402-85-7 211509-29-4, Protein (human clone KIAA0626
 reduced) 212701-83-2, Antigen JTT.1 (human) 213471-70-6, Protein
 zsig32 (human) 213537-31-6 221369-74-0 222536-56-3 222614-92-8
 222963-77-1, Protein (human brain gene KIAA0879) 225371-37-9
 227183-97-3 228856-39-1 228859-29-8, Protein (human gene PG1)
 229483-48-1 229483-74-3 229965-62-2 234086-26-1 235768-74-8
 236732-55-1 243122-23-8 243122-49-8 244028-96-4 244295-44-1
 249910-22-3 250154-03-1 251929-91-6 252050-85-4 252051-18-6
 252051-68-6 252366-50-0 252366-55-5 253418-72-3 253418-75-6
 253418-83-6 253419-18-0 253419-34-0 253419-41-9 253603-07-5
 256325-28-7 257854-54-9 259163-54-7 259163-79-6 260382-31-8
 270051-56-4, Hydrolase (human Incyte clone 1297034) 270051-58-6,
 Hydrolase (human Incyte clone 1702211) 270054-17-6, Platelet-derived
 growth factor D (human) 271753-29-8 277336-39-7 277762-05-7
 278626-74-7, Osteoglycin (human gene OGN) 287216-11-9 291585-61-0
 291797-63-2 292066-57-0 292656-62-3 292658-62-9 292883-48-8
 293308-26-6 294683-12-8 294900-23-5 294906-53-9 297774-95-9
 300429-08-7 300431-40-7 300619-65-2 300620-75-1 301252-55-1
 301257-58-9 303071-71-8 309763-61-9 312976-96-8 314326-43-7
 318300-05-9, Protein (human clone PSEC0021) 318301-14-3, Protein (human
 clone PSEC0133) 318301-24-5, Protein (human clone PSEC0143)
 318301-57-4, Protein (human clone PSEC0170) 321452-27-1 321452-28-2
 321452-29-3 321452-30-6 321452-31-7 321452-32-8 321452-33-9

321452-34-0	321452-35-1	321452-36-2	321452-37-3	321452-38-4
321452-39-5	321452-40-8	321452-41-9	321452-42-0	321452-43-1
321452-44-2	321452-45-3	321452-46-4	321452-47-5	321452-48-6
321574-52-1	321574-56-5	321574-57-6	321574-70-3	321862-39-9
321862-44-6	321862-47-9	325502-00-9	326501-86-4	326501-87-5
326501-88-6	326501-89-7	326501-90-0	326501-91-1	326501-92-2
326501-93-3	326501-94-4	326501-95-5	326501-96-6	326501-97-7
326501-98-8	326501-99-9	326502-00-5	326502-01-6	326502-31-2
326502-32-3	326502-33-4	326502-34-5	326502-35-6	326502-36-7
326502-37-8	326502-38-9	326502-39-0	326502-40-3	326502-41-4
326502-42-5	326502-43-6	326598-27-0	326598-44-1	326598-72-5
326598-76-9	326598-78-1	326598-79-2	326598-80-5	326598-81-6
326598-82-7	326598-84-9	326833-56-1	326833-60-7	326833-66-3
326930-69-2,	Protein (human (human clone MAMMA1001388)	clone PLACE1010800)	326941-34-8, Protein	
			328596-84-5	328596-85-6
328596-87-8	328596-88-9	328596-89-0	328596-90-3	328596-91-4
328596-92-5	328596-93-6	328596-94-7	328596-95-8	328596-96-9
328596-97-0	328596-98-1	328596-99-2	328597-00-8	328597-01-9
328597-02-0	328597-03-1	328597-04-2	328597-05-3	328597-06-4
328597-07-5	328597-08-6	328597-09-7	328597-10-0	328597-11-1
328597-12-2	328597-13-3	328597-14-4	328597-15-5	328597-16-6
328597-17-7	328597-18-8	328597-19-9	328597-20-2	328597-21-3
328908-57-2	328908-94-7	328909-30-4	328909-65-5	328910-79-8
328911-22-4	328911-58-6	328911-95-1	328912-59-0	328912-60-3
328912-61-4	330226-44-3	330226-45-4	330226-46-5	330226-47-6
330226-48-7	330226-49-8	330226-50-1	330226-51-2	330226-52-3
330226-53-4	330226-54-5	330226-55-6	330226-56-7	330226-57-8
330226-58-9	330226-59-0	330226-60-3	330226-61-4	330226-62-5
330226-63-6	330226-64-7	330226-65-8	330226-66-9	330226-67-0
330226-68-1	330226-69-2	330226-70-5	330226-71-6	330226-72-7
330226-73-8	330226-74-9	330226-75-0		

RL: PRP (Properties)

(unclaimed protein sequence; albumin fusion proteins with therapeutic
proteins for improved shelf-life)

IT	330226-76-1	330226-77-2	330226-78-3	330226-79-4	330226-80-7
	330226-81-8	330226-82-9	330226-83-0	330226-84-1	330226-85-2
	330226-86-3	330226-87-4	330226-88-5	330226-89-6	330226-90-9
	330437-94-0	330437-95-1	330437-96-2	330437-97-3	330437-98-4
	330437-99-5	332903-21-6	334569-82-3	335366-30-8	337542-34-4
	337542-35-5	337542-36-6	337542-37-7	337542-38-8	337542-39-9
	337542-40-2	337542-41-3	337542-42-4	337542-43-5	337542-44-6
	337542-45-7	337542-46-8	337542-47-9	337542-48-0	337542-49-1
	337542-50-4	337542-51-5	337542-52-6	337542-53-7	337542-54-8
	337542-55-9	337542-56-0	337542-57-1	337542-58-2	337542-59-3
	337542-60-6	337961-06-5	337961-07-6	337961-09-8	337961-10-1
	337961-60-1	337961-74-7	337961-77-0	337961-78-1	337961-79-2
	337961-81-6	337961-82-7	337961-85-0	337961-86-1	337961-87-2
	337961-88-3	337986-88-6	337986-89-7	337986-90-0	337986-91-1
	337986-92-2	337986-93-3	337986-94-4	337986-95-5	337986-96-6
	337986-97-7	337986-98-8	338412-71-8	338412-97-8	338413-32-4
	338413-67-5	338413-99-3	338414-30-5	338414-74-7	338415-04-6
	338415-31-9	339139-34-3	339139-35-4	339139-36-5	339139-37-6
	339139-38-7	339139-39-8	339139-40-1	339139-41-2	339139-42-3
	339139-43-4	339139-44-5	339139-45-6	339140-43-1	339140-44-2
	339140-45-3	339140-46-4	339140-47-5	339140-48-6	339140-49-7
	339140-50-0	339140-51-1	339140-52-2	339140-53-3	339140-54-4
	339140-55-5	339140-56-6	339140-57-7	339140-58-8	339140-59-9
	339140-60-2	339140-61-3	339140-62-4	339140-63-5	339140-64-6
	339140-65-7	339140-66-8	339140-67-9	339140-68-0	339140-69-1
	339140-70-4	339140-71-5	339140-72-6	339140-73-7	339140-74-8
	339143-87-2	339143-88-3	339143-89-4	339143-90-7	339143-91-8
	339143-92-9	339143-93-0	339143-94-1	339143-95-2	339143-96-3
	339143-97-4	339143-98-5	339143-99-6	339144-00-2	339144-01-3

339144-02-4	339144-03-5	339144-04-6	339144-05-7	339144-06-8
339144-07-9	339144-08-0	339144-09-1	339144-10-4	339144-11-5
339144-12-6	339144-13-7	339144-14-8	339144-15-9	339144-16-0
339144-17-1	339144-18-2	339144-19-3	339144-20-6	339144-21-7
339144-22-8	339144-23-9	339144-24-0	339144-25-1	339144-26-2
339144-27-3	339180-59-5	339180-64-2	339180-65-3	339180-66-4
339180-67-5	339180-68-6	339180-70-0	339180-71-1	339180-72-2
339180-73-3	339180-74-4	339180-75-5	339180-77-7	339180-79-9
339180-80-2	339180-84-6	339181-12-3	339181-13-4	339181-14-5
339181-15-6	339181-16-7	339181-18-9	339181-19-0	339181-21-4
339181-40-7	339181-41-8	339181-42-9	339181-43-0	339181-49-6
339181-58-7	339181-81-6	339182-04-6	339182-61-5	339182-63-7
339182-72-8	339182-83-1	339213-16-0	339213-17-1	339213-18-2
339213-19-3	339213-20-6	339213-21-7	339213-22-8	339213-23-9
339213-24-0	339213-25-1	339213-26-2	339213-27-3	339213-28-4
339213-29-5	339213-30-8	339213-31-9	339213-32-0	339213-33-1
339213-34-2	339213-35-3	339213-36-4	339213-37-5	339213-38-6
339213-39-7	339213-40-0	339213-41-1	339213-42-2	339213-43-3
339213-44-4	339213-45-5	339213-46-6	339213-47-7	339216-27-2

RL: PRP (Properties)

(unclaimed protein sequence; albumin fusion proteins with therapeutic
proteins for improved shelf-life)

IT	339216-28-3	339216-29-4	339216-30-7	339216-31-8	339216-32-9
	339216-33-0	339216-34-1	339216-35-2	339216-36-3	339216-37-4
	339216-38-5	339216-39-6	339216-40-9	339216-41-0	339216-42-1
	339216-43-2	339216-44-3	339216-45-4	339216-46-5	339216-47-6
	339216-48-7	339216-49-8	339216-50-1	339216-51-2	339216-52-3
	339216-53-4	339216-54-5	339216-55-6	339216-56-7	339216-57-8
	339216-58-9	339216-59-0	339216-60-3	339216-61-4	339216-62-5
	339216-63-6	339216-64-7	339216-65-8	339216-66-9	339216-67-0
	339216-68-1	339301-12-1	339301-15-4	339301-17-6	339301-82-5
	339301-83-6	339301-84-7	339301-90-5	339302-01-1	339302-11-3
	339302-22-6	339302-36-2	339302-46-4	339302-57-7	339302-68-0
	339302-78-2	339302-95-3	339303-22-9	339596-82-6	339596-83-7
	339596-84-8	339596-85-9	339596-86-0	339596-87-1	339596-88-2
	339596-89-3	339596-90-6	339596-91-7	339596-92-8	339596-95-1
	339596-96-2	339596-97-3	339596-99-5	339597-00-1	339597-01-2
	339597-02-3	339597-03-4	339597-04-5	339597-05-6	339597-06-7
	339597-07-8	339597-08-9	339597-09-0	339597-10-3	339597-11-4
	339597-12-5	339597-13-6	339597-14-7	339602-78-7	339602-79-8
	339602-80-1	339602-81-2	339602-82-3	339602-83-4	339602-84-5
	339602-85-6	339602-86-7	339602-87-8	339602-88-9	339602-89-0
	339602-90-3	339602-91-4	339602-92-5	339602-93-6	339602-94-7
	339602-95-8	339602-96-9	339602-97-0	339602-98-1	339602-99-2
	339603-00-8	339603-01-9	339603-02-0	339603-03-1	339603-04-2
	339603-05-3	339603-06-4	339603-07-5	339603-08-6	339603-09-7
	339603-65-5	339603-66-6	339603-67-7	339603-68-8	339603-69-9
	339603-70-2	339603-71-3	339603-72-4	339603-73-5	339603-74-6
	339603-75-7	339603-76-8	339603-77-9	339603-78-0	339603-79-1
	339605-81-1	339605-82-2	339605-83-3	339605-84-4	339605-86-6
	339605-87-7	339605-88-8	339605-89-9	339605-90-2	339605-91-3
	339605-92-4	339605-93-5	339605-94-6	339605-95-7	339605-96-8
	339605-97-9	339605-98-0	339605-99-1	339606-00-7	339606-01-8
	339607-60-2	339607-61-3	339607-62-4	339607-63-5	339607-64-6
	339607-65-7	339607-66-8	339607-67-9	339607-68-0	339607-69-1
	339607-70-4	339609-39-1	339609-40-4	339609-41-5	339609-42-6
	339609-43-7	339609-44-8	339609-45-9	339609-46-0	339609-47-1
	339609-48-2	339609-49-3	339609-50-6	339609-51-7	339609-52-8
	339609-53-9	339609-54-0	339609-55-1	339609-56-2	339609-58-4
	339609-59-5	339609-60-8	339609-61-9	339609-62-0	339610-43-4
	339610-44-5	339610-45-6	339610-46-7	339610-47-8	339610-48-9
	339610-49-0	339610-50-3	339610-51-4	339610-52-5	339610-53-6
	339610-54-7	339610-55-8	339610-56-9	339610-57-0	339610-58-1

339610-59-2 339610-60-5 339610-61-6 339610-62-7 339610-63-8
 339610-64-9 339611-78-8 339611-79-9 339611-80-2 339611-81-3
 339611-82-4 339611-83-5 339611-84-6 339611-85-7 339611-86-8
 339611-87-9 339611-88-0 339611-89-1 339611-90-4 339611-91-5
 339611-92-6 339611-93-7 339611-94-8 339611-95-9 339611-96-0
 339611-97-1 339611-98-2 339611-99-3 339612-00-9 339612-01-0
 339612-89-4 339612-90-7 339612-91-8 339612-92-9 339612-93-0

RL: PRP (Properties)

(unclaimed protein sequence; albumin fusion proteins with therapeutic
proteins for improved shelf-life)

IT 339612-94-1 339612-95-2 339612-96-3 339612-97-4 339612-98-5
 339612-99-6 339613-00-2 339613-01-3 339613-02-4 339613-03-5
 339613-04-6 339613-05-7 339613-06-8 339613-07-9 339613-08-0
 339613-88-6 339613-89-7 339613-90-0 339613-91-1 339613-92-2
 339613-94-4 339613-95-5 339613-96-6 339613-97-7 339613-98-8
 339613-99-9 339614-00-5 339614-01-6 339614-02-7 339614-03-8
 339614-04-9 339614-05-0 339614-06-1 339614-07-2 339614-08-3
 339614-09-4 339614-10-7 339614-11-8 339614-12-9 339614-13-0
 339614-14-1 339614-15-2 339614-16-3 339614-17-4 339614-18-5
 339614-19-6 339614-20-9 339614-21-0 339614-22-1 339614-23-2
 339614-24-3 339616-76-1 340011-23-6 340011-25-8 340011-27-0
 340011-29-2 340011-38-3 340011-41-8 340011-73-6 340011-77-0
 340012-12-6 340012-94-4 340012-96-6 340012-99-9 340013-00-5
 340013-18-5 340013-32-3 340013-72-1 340013-83-4 340013-84-5
 340013-85-6 340013-87-8 340013-89-0 340013-91-4 340014-06-4
 340014-08-6 340014-10-0 340014-11-1 340014-12-2 340014-15-5
 340014-16-6 340014-17-7 340014-20-2 340014-21-3 340014-23-5
 340014-24-6 340014-26-8 340014-29-1 340014-37-1 340014-90-6
 340015-01-2 340015-03-4 340015-15-8 340015-19-2 340015-23-8
 340015-28-3 340015-29-4 340015-30-7 340015-35-2 340015-38-5
 340015-40-9 340015-42-1 340015-45-4 340015-46-5 340015-47-6
 340015-48-7 340015-49-8 340015-50-1 340015-51-2 340015-52-3
 340015-53-4 340015-54-5 340015-55-6 340015-56-7 340015-62-5
 340016-14-0 340016-16-2 340016-18-4 340016-37-7 340016-40-2
 340016-43-5 340016-44-6 340016-49-1 340016-55-9 340016-64-0
 340016-66-2 340016-75-3 340016-84-4 340016-87-7 340016-94-6
 340016-95-7 340016-96-8 340016-98-0 340017-00-7 340017-04-1
 340017-06-3 340017-08-5 340017-09-6 340017-10-9 340017-11-0
 340017-12-1 340017-13-2 340017-32-5 340017-38-1 340017-39-2
 340018-35-1 340018-80-6 340018-87-3 340018-92-0 340018-93-1
 340018-94-2 340018-95-3 340018-96-4 340019-02-5 340019-04-7
 340019-05-8 340020-74-8 340020-76-0 340020-77-1 340020-78-2
 340020-80-6 340021-34-3 340022-03-9 340022-34-6 340022-78-8
 340023-19-0 340023-31-6 340023-33-8 340023-34-9 340023-35-0
 340023-36-1 340023-37-2 340023-39-4 340023-41-8 340023-42-9
 340023-45-2 340023-46-3 340023-57-6 340023-87-2 340024-09-1
 340024-30-8 340024-35-3 340024-39-7 340024-58-0 340024-79-5
 340026-04-2 340050-60-4 340050-61-5 340050-62-6 340050-63-7
 340050-64-8 340050-65-9 340050-66-0 340050-67-1 340050-68-2
 340050-69-3 340050-70-6 340050-71-7 340050-72-8 340050-73-9
 340050-74-0 340050-75-1 340050-76-2 340050-77-3 340050-78-4
 340050-79-5 340050-80-8 340050-81-9 340050-82-0 340050-83-1
 340050-84-2 340050-85-3 340050-86-4 340050-87-5 340050-88-6
 340050-89-7 340050-90-0 340050-91-1 340050-92-2 340161-11-7
 340161-25-3 340161-26-4 340161-27-5 340161-28-6 340161-29-7
 340161-30-0 340161-47-9 340161-72-0 340161-73-1 340161-74-2
 340161-77-5 340161-78-6 340161-79-7 340161-80-0 340161-89-9
 340161-90-2 340161-91-3 340838-03-1 340838-04-2 340838-05-3

RL: PRP (Properties)

(unclaimed protein sequence; albumin fusion proteins with therapeutic
proteins for improved shelf-life)

IT 340838-06-4 340838-07-5 340838-08-6 340838-09-7 340838-10-0
 340838-11-1 340838-12-2 340838-13-3 340838-14-4 340838-15-5

340838-16-6	340838-17-7	340838-18-8	340838-19-9	340838-20-2
340838-21-3	340838-22-4	340838-23-5	340838-24-6	340838-25-7
340838-26-8	340838-27-9	340839-86-3	340983-53-1	340983-54-2
341065-94-9	341065-95-0	341065-96-1	341065-97-2	341065-98-3
341065-99-4	341066-00-0	341066-01-1	341066-02-2	341066-03-3
341066-04-4	341066-05-5	341066-06-6	341066-07-7	341066-08-8
341066-09-9	341066-10-2	341066-11-3	341066-12-4	341066-13-5
341066-14-6	341066-15-7	341066-16-8	341066-17-9	341066-18-0
341066-19-1	341066-20-4	341066-21-5	341066-22-6	341066-23-7
341066-24-8	341066-25-9	341066-26-0	341066-27-1	341066-28-2
341066-29-3	341066-30-6	341523-23-7	341523-25-9	343901-47-3
346013-08-9	352395-92-7	352395-93-8	352395-94-9	352395-95-0
352395-96-1	352395-97-2	352395-99-4	352396-00-0	352396-01-1
352396-02-2	352396-03-3	352396-04-4	352396-05-5	352396-06-6
352396-07-7	352396-08-8	352396-09-9	352396-10-2	352396-11-3
352396-12-4	352396-13-5	352396-14-6	352396-15-7	352396-16-8
352396-17-9	352396-18-0	352396-19-1	352396-22-6	352396-23-7
352396-24-8	352396-25-9	352396-26-0	352396-27-1	352396-28-2
352396-29-3	352396-30-6	352396-31-7	352396-32-8	352401-89-9
352433-90-0	352434-21-0	352434-34-5	353341-91-0	353341-92-1
353341-93-2	353341-94-3	353341-95-4	353341-96-5	353341-97-6
353341-98-7	353341-99-8	353342-00-4	353342-01-5	353342-02-6
353342-03-7	353342-04-8	353342-05-9	353342-06-0	353342-07-1
353342-08-2	353342-09-3	353342-10-6	353342-11-7	353520-00-0
353520-07-7	353552-65-5	355045-10-2	368438-96-4	368441-51-4
368441-54-7	368441-64-9	368441-73-0	368441-93-4	368442-77-7
368442-78-8	368442-79-9	368442-83-5	368442-84-6	368442-85-7
368442-86-8	368442-93-7	368442-97-1	368442-98-2	368442-99-3
368443-00-9	368443-01-0	368443-02-1	368443-11-2	368443-20-3
368443-21-4	368443-22-5	368443-23-6	368443-24-7	368443-26-9
368443-30-5	368443-31-6	368443-32-7	368443-34-9	368443-35-0
368443-36-1	368443-39-4	368443-40-7	368443-41-8	368443-43-0
368443-44-1	368443-45-2	368443-46-3	368443-47-4	368443-48-5
368443-49-6	368443-67-8	368443-80-5	368443-86-1	368443-87-2
368443-88-3	368443-89-4	368443-96-3	368443-97-4	368443-99-6
368941-46-2	368941-47-3	368941-48-4	368941-49-5	368941-50-8
368941-51-9	368941-52-0	368941-53-1	368941-54-2	368941-55-3
368941-56-4	368941-57-5	368941-58-6	368941-59-7	368941-60-0
368941-61-1	368941-62-2	368941-63-3	368941-65-5	368941-66-6
368941-67-7	368941-68-8	368941-70-2	368941-71-3	368941-72-4
368941-73-5	368941-74-6	368941-75-7	368941-76-8	368941-77-9
368941-78-0	368941-79-1	368941-80-4	368941-81-5	368941-82-6
368941-83-7	368941-84-8	368941-85-9	368941-86-0	368941-88-2
368941-89-3	368941-90-6	368941-91-7	368941-92-8	368941-93-9
368941-94-0	368941-95-1	368941-96-2	368941-97-3	368941-98-4
368941-99-5	368942-00-1	368942-01-2	368942-02-3	368942-03-4

RL: PRP (Properties)

(unclaimed protein sequence; albumin fusion proteins with therapeutic
proteins for improved shelf-life)

IT	368942-04-5	368942-05-6	368942-07-8	368942-08-9	368942-09-0
	368942-10-3	368942-12-5	368942-13-6	368942-14-7	368942-15-8
	368942-16-9	368942-18-1	368942-19-2	368942-22-7	368942-23-8
	368942-24-9	368942-25-0	368942-26-1	368942-27-2	368942-28-3
	368942-29-4	368942-31-8	368942-32-9	368942-33-0	368942-34-1
	368942-35-2	368942-36-3	368942-38-5	368942-39-6	368942-40-9
	368942-42-1	368942-43-2	368942-44-3	368942-45-4	368942-47-6
	368942-48-7	368942-49-8	368942-50-1	368942-52-3	368942-53-4
	368942-54-5	368942-55-6	368942-56-7	368942-57-8	368942-58-9
	368942-59-0	368942-60-3	368942-61-4	368942-63-6	368942-64-7
	368942-65-8	368942-66-9	368942-67-0	368942-68-1	368942-69-2
	368942-70-5	368942-71-6	368942-73-8	368942-74-9	368942-75-0
	368942-76-1	368942-77-2	368942-79-4	368942-80-7	368942-82-9
	368942-83-0	368942-85-2	368942-86-3	368942-87-4	368942-88-5

368942-89-6	368942-90-9	368942-91-0	368942-92-1	368942-93-2
368942-94-3	368942-95-4	368942-96-5	368942-97-6	368942-98-7
368942-99-8	368943-00-4	368943-01-5	368943-02-6	368943-03-7
368943-04-8	368943-05-9	368943-06-0	368943-07-1	368943-08-2
368943-10-6	368943-11-7	368943-12-8	368943-13-9	368943-14-0
368943-15-1	368943-16-2	368943-17-3	368943-18-4	368943-20-8
368943-21-9	368943-22-0	368943-23-1	368943-24-2	368943-26-4
368943-28-6	368943-29-7	368943-32-2	368943-33-3	368943-34-4
368943-35-5	368943-36-6	368943-37-7	368943-38-8	368943-39-9
368943-40-2	368943-41-3	368943-42-4	368943-43-5	368943-44-6
368943-45-7	368943-46-8	368943-47-9	368943-48-0	368943-49-1
368943-50-4	368943-51-5	368943-52-6	368943-53-7	368943-54-8
368943-55-9	368943-56-0	368943-57-1	368943-59-3	368943-60-6
368943-62-8	368943-63-9	368943-64-0	368943-65-1	368943-66-2
369413-73-0	369413-74-1	369413-75-2	369413-76-3	369413-77-4
369413-78-5	369413-80-9	369413-81-0	369413-82-1	369413-83-2
369413-84-3	369413-85-4	369413-86-5	369413-87-6	369413-88-7
369413-89-8	369413-90-1	369413-91-2	369413-92-3	369413-93-4
369413-94-5	369413-95-6	369413-96-7	369413-97-8	369413-98-9
369413-99-0	369414-00-6	369414-01-7	369414-02-8	369414-03-9
369414-04-0	369414-05-1	369414-06-2	369414-07-3	369414-08-4
369414-09-5	369414-10-8	369414-11-9	369414-12-0	369414-13-1
369414-14-2	369414-15-3	369414-16-4	369414-17-5	369414-18-6
369414-19-7	369414-20-0	369414-21-1	369414-22-2	369414-23-3
369414-24-4	369414-25-5	369414-26-6	369414-27-7	369414-28-8
369414-29-9	369414-30-2	369414-31-3	369414-32-4	369414-33-5
369414-34-6	369414-35-7	369414-36-8	369414-37-9	369414-38-0
369414-39-1	369414-40-4	369414-41-5	369414-42-6	369414-43-7
369414-44-8	369414-45-9	369414-46-0	369414-47-1	369414-48-2
369414-49-3	369414-50-6	369414-51-7	369414-53-9	369414-54-0
369414-55-1	369414-56-2	369414-57-3	369414-58-4	369414-59-5
369414-60-8	369414-61-9	369414-62-0	369414-63-1	369414-64-2
369414-65-3	369414-66-4	369414-67-5	369414-68-6	369414-69-7
369414-70-0	369414-71-1	369414-72-2	369414-73-3	369414-74-4

RL: PRP (Properties)

(unclaimed protein sequence; albumin fusion proteins with therapeutic
proteins for improved shelf-life)

IT	369414-75-5	369414-76-6	369414-77-7	369414-78-8	369414-79-9
	369414-80-2	369414-81-3	369414-82-4	369414-83-5	369414-84-6
	369414-85-7	369414-86-8	369414-87-9	369414-88-0	369414-89-1
	369414-90-4	369414-91-5	369414-92-6	369414-93-7	369414-94-8
	369414-95-9	369414-96-0	369414-97-1	369414-98-2	369414-99-3
	369415-00-9	369415-01-0	369415-02-1	369415-03-2	369415-04-3
	369415-05-4	369415-06-5	369415-07-6	369415-08-7	369415-09-8
	369415-10-1	369415-11-2	369415-12-3	369415-13-4	369415-14-5
	369415-15-6	369415-16-7	369415-17-8	369415-18-9	369415-19-0
	369415-20-3	369415-21-4	369415-22-5	369415-23-6	369415-24-7
	369415-25-8	369415-26-9	369415-27-0	369415-28-1	369415-29-2
	369415-30-5	369415-31-6	369415-32-7	369415-33-8	369415-34-9
	369415-35-0	369415-36-1	369415-37-2	369415-38-3	369415-39-4
	369415-40-7	369415-41-8	369415-42-9	369415-43-0	369415-44-1
	369415-45-2	369415-46-3	369415-47-4	369415-48-5	369415-49-6
	369415-50-9	369415-51-0	369415-52-1	369415-53-2	369415-54-3
	369415-55-4	369415-56-5	369415-57-6	369415-58-7	369415-59-8
	369415-60-1	369631-86-7	369631-87-8	369631-88-9	369631-89-0
	369631-94-7	369632-03-1	369632-04-2	369632-05-3	369632-06-4
	369632-07-5	369632-08-6	369632-10-0	369632-11-1	369632-19-9
	369632-28-0	369632-47-3	369632-51-9	369632-53-1	369632-54-2
	369632-74-6	369632-76-8	369632-86-0	369632-87-1	369632-88-2
	369632-89-3	369638-47-1	369638-48-2	369638-49-3	369638-50-6
	369638-51-7	369638-52-8	369638-53-9	369638-54-0	369638-55-1
	369638-56-2	369638-57-3	369638-58-4	369638-59-5	369638-77-7
	369638-84-6	369638-85-7	369638-86-8	369638-89-1	369638-90-4

369638-91-5	369638-92-6	369638-93-7	369638-94-8	369638-95-9
369638-96-0	369638-97-1	369638-98-2	369638-99-3	369639-00-9
369639-01-0	369639-02-1	369639-03-2	369639-04-3	369639-06-5
369639-07-6	369639-09-8	369639-10-1	369639-11-2	369639-13-4
369639-16-7	369639-17-8	369639-23-6	369639-27-0	369639-30-5
369639-31-6	369639-35-0	369639-39-4	369639-50-9	369639-61-2
369639-70-3	369639-77-0	369639-81-6	369639-92-9	369640-00-6
369640-11-9	369640-26-6	369642-09-1	369642-27-3	369642-45-5
369642-62-6	369642-78-4	369642-97-7	369643-07-2	369643-17-4
369643-26-5	369643-40-3	369644-05-3	369644-17-7	369644-35-9
369644-48-4	369644-58-6	369644-62-2	369644-63-3	369644-64-4
369644-69-9	369644-70-2	369644-72-4	369644-73-5	369644-74-6
369644-76-8	369644-77-9	369644-78-0	369644-79-1	370068-85-2

RL: PRP (Properties)

(unclaimed protein sequence; albumin fusion proteins with therapeutic
proteins for improved shelf-life)

IT	122024-47-9	131748-18-0	217893-85-1,	GenBank A63622	222404-09-3
	251343-93-8	295783-43-6	328529-69-7	330179-08-3	337459-95-7
	337459-96-8	337459-97-9	337459-98-0	337459-99-1	337460-00-1
	337460-01-2	337460-02-3	337460-03-4	337460-04-5	337939-20-5
	338949-18-1	339073-57-3	339073-58-4	339073-59-5	339073-60-8
	339073-61-9	339073-62-0	339073-63-1	339079-35-5	339079-36-6
	339079-37-7	339079-38-8	339079-39-9	339079-40-2	339079-41-3
	339079-42-4	339079-43-5	339079-44-6	339079-45-7	339079-46-8
	339079-47-9	339079-48-0	339148-16-2	339148-17-3	339148-18-4
	339148-19-5	339148-20-8	339148-21-9	339148-22-0	339148-23-1
	339148-24-2	339148-25-3	339148-26-4	339175-34-7	339266-46-5
	339266-47-6	339266-48-7	339266-49-8	339266-50-1	339266-52-3
	339266-53-4	339266-54-5	339266-55-6	339266-56-7	339266-57-8
	339266-58-9	339266-59-0	339523-99-8	339524-00-4	339524-01-5
	339524-02-6	339524-03-7	339524-04-8	339524-05-9	339524-06-0
	339524-07-1	339524-08-2	339524-09-3	339524-10-6	339524-79-7
	339524-80-0	339524-81-1	339524-82-2	339524-83-3	339524-84-4
	339524-85-5	339524-86-6	339524-87-7	339524-88-8	339524-89-9
	339524-90-2	339524-91-3	339524-92-4	339526-31-7	339526-32-8
	339526-33-9	339526-34-0	339526-35-1	339526-36-2	339526-37-3
	339526-38-4	339526-39-5	339526-40-8	339526-41-9	339526-42-0
	339526-43-1	339526-44-2	339526-45-3	339526-46-4	339526-47-5
	339526-48-6	339526-49-7	339527-59-2	339529-52-1	339529-55-4
	339529-56-5	339529-57-6	339529-58-7	339529-59-8	339529-60-1
	339529-61-2	339529-62-3	339529-64-5	339529-65-6	339540-74-8
	339540-75-9	339540-76-0	339540-77-1	339540-78-2	339540-79-3
	339540-80-6	339540-81-7	339540-82-8	339540-83-9	339541-20-7
	339541-21-8	339541-23-0	339541-24-1	339541-25-2	339541-26-3
	339541-27-4	339541-28-5	339565-68-3	339605-85-5	339613-93-3
	340003-40-9	340003-41-0	340003-42-1	340003-43-2	340003-44-3
	340003-45-4	340003-46-5	340003-47-6	340003-48-7	340255-72-3
	340255-74-5	340255-75-6	340255-76-7	340255-77-8	340255-78-9
	340255-79-0	340255-80-3	340255-81-4	340255-82-5	340255-83-6
	340255-84-7	340256-43-1	340685-59-8	340773-66-2	340963-10-2
	340963-11-3	352273-69-9	352273-70-2	353264-67-2	353264-68-3
	367273-46-9	367273-47-0	367273-48-1	368941-64-4	368941-69-9
	368941-87-1	368942-06-7	368942-11-4	368942-17-0	368942-20-5
	368942-21-6	368942-30-7	368942-37-4	368942-41-0	368942-46-5
	368942-51-2	368942-62-5	368942-72-7	368942-78-3	368942-81-8
	368942-84-1	368943-09-3	368943-19-5	368943-25-3	368943-27-5
	368943-30-0	368943-31-1	368943-58-2	368943-61-7	369386-27-6
	369386-99-2	369387-03-1	369413-79-6	369414-52-8	369589-20-8
	369593-28-2	369593-29-3	369593-30-6	369593-33-9	369593-41-9
	369593-44-2	369593-45-3	369593-46-4	369638-87-9	369660-66-2

RL: PRP (Properties)

(unclaimed sequence; albumin fusion proteins with therapeutic proteins
for improved shelf-life)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Delta Biotechnology Limited; EP 0322094 A1 1989 HCPLUS
- (2) Delta Biotechnology Limited; WO 9724445 A1 1997 HCPLUS
- (3) Human Genome Sciences Inc; WO 9734997 A1 1997 HCPLUS

L66 ANSWER 12 OF 29 HCPLUS COPYRIGHT 2004 ACS on STN

AN 2000:609058 HCPLUS

DN 133:168425

ED Entered STN: 01 Sep 2000

TI Suppository of **recombinant** human **interferon**.

alpha.2a

IN Chen, Weijia; Zheng, Hui; Zhang, Yan; Wang, Dongqian

PA Changchun Biological Product Inst., Ministry of Public Health, Peop. Rep. China

SO Faming Zhuanli Shengqing Gongkai Shuomingshu, 5 pp.

CODEN: CNXXEV

DT Patent

LA Chinese

IC ICM A61K009-02

ICS A61K038-21

CC 63-6 (Pharmaceuticals)

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	-----	-----	-----	-----
PI CN 1230400	A	19991006	CN 1999-105589	19990415 <--

PRAI CN 1999-105589 19990415 <--

AB Suppository of **interferon** α 2a comprise
recombinant human **interferon** α 2a solution
(0.5 MIU per suppository) 14, glycerol 58, gelatin 26, and human serum
albumin 2%. The preparation process involves mixing glycerol with
gelatin, standing overnight, sterilizing for 20-30 min, cooling to
40-56°, adding **recombinant** human **interferon**.
alpha.2a, and shaping.

ST **recombinant** human **interferon** **alpha** 2a
suppository

IT **Albumins, biological studies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(serum; suppository of **recombinant** human **interferon**
 α 2a)

IT Drug delivery systems
(suppositories; suppository of **recombinant** human
interferon α 2a)

IT **Anti-inflammatory** agents
Antitumor agents
Antiviral agents
Skin, disease
(suppository of **recombinant** human **interferon**
 α 2a)

IT Gelatins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(suppository of **recombinant** human **interferon**
 α 2a)

IT **Interferons**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α -2a, **recombinant** human;
suppository of **recombinant** human **interferon**
 α 2a)

IT 56-81-5, Glycerol, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(suppository of **recombinant** human **interferon**
 α 2a)

L66 ANSWER 13 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:783954 HCAPLUS

DN 132:26853

ED Entered STN: 10 Dec 1999

TI Recombinant human **interferon β -1A (IFN-beta-1A)** formulation

IN Alam, John; Rogge, Mark; Goelz, Susan

PA Biogen, Inc., USA

SO PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K038-21

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 15

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9962542	A1	19991209	WO 1998-US7242	19980529 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2333063	AA	19991209	CA 1998-2333063	19980529 <--
	AU 9888225	A1	19991220	AU 1998-88225	19980529 <--
	BR 9815966	A	20010228	BR 1998-15966	19980529 <--
	EP 1082132	A1	20010314	EP 1998-939859	19980529 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002516874	T2	20020611	JP 2000-551797	19980529 <--
	EE 2000000694	A	20020617	EE 2000-20000069419980529	<--
	NO 20000006022	A	20010126	NO 2000-6022	20001128 <--

PRAI WO 1998-US7242 A 19980529 <--

AB Liquid compns. comprising a buffer of pH about 7.2, **recombinant interferon-β** and 15 mg/mL of human serum **albumin**, and kits for parenteral administration comprising said compns. are disclosed.

ST **recombinant interferon beta** formulation

IT Medical goods

(alc. swabs; **recombinant human interferon β -1A (IFN-beta-1A)** formulation)

IT Medical goods

(bandages, adhesive; **recombinant human interferon β -1A (IFN-beta-1A)** formulation)

IT Buffers

Molecular cloning

Needles (tools)

Syringes

pH

(**recombinant human interferon β -1A (IFN-beta-1A)** formulation)

IT **Albumins, biological studies**

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(serum, human; **recombinant human interferon β -1A (IFN-beta-1A)** formulation)

IT **Interferons**

RL: BPN (Biosynthetic preparation); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); PROC (Process); USES (Uses)
 (β ; recombinant human **interferon**
 β -1A (IFN-beta-1A) formulation)

IT 145258-61-3, **Interferon β 1** (human fibroblast
 protein moiety)
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
 use); BIOL (Biological study); PROC (Process); USES (Uses)
 (recombinant human **interferon β -1A** (IFN-beta-1A) formulation)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Alam, J; Pharmaceutical Research 1997, V14(4), P546 HCPLUS
- (2) Anon; http://www.healthdirect.com/usenew/pressrel/p_biogel.htm 1996
- (3) Salmon, P; Journal of Interferon and Cytokine Research 1996, V16(10), P759 HCPLUS
- (4) US Food and Drug Administration-Interferon Beta-1A, Biogen, Inc;
<http://www.fda.gov/cber/products/ifnbbio051796.htm>,
<http://www.fda.gov/cber/label/infbbio051796lb.pdf> 1998

L66 ANSWER 14 OF 29 HCPLUS COPYRIGHT 2004 ACS on STN

AN 1999:563880 HCPLUS

DN 131:161626

ED Entered STN: 08 Sep 1999

TI Oral **recombinant** human α -**interferon**

compositions

IN Dong, Yilan; Cheng, Xiaogeng; Lin, Yuxin; Wang, Shiwen; Liu, Zhenhao;
 Duan, Li

PA Changchun Institute of Biological Products, Ministry of Public Health,
 Peop. Rep. China

SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 8 pp.

CODEN: CNXXEV

DT Patent

LA Chinese

IC ICM A61K038-21

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 15

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CN 1116951	A	19960221	CN 1995-101216	19950125 <--
PRAI	CN 1995-101216		19950125 <--		

AB Title compns. as antiviral agents contain **recombinant** human α -**interferon** 100-500 IU, thymosin F5 isolated from calf's thymus gland 1-20 µg, stabilizers and conventional medical additives. The stabilizers are selected from human serum **albumin**, cattle serum **albumin**, β-cyclodextrin and PEG 800.

ST **recombinant** human **interferon** tablet antiviral

IT Antiviral agents

Stabilizing agents

(oral **recombinant** human α -**interferon** compns.)

IT Polyoxyalkylenes, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (oral **recombinant** human α -**interferon** compns.)

IT Drug delivery systems

(oral; oral **recombinant** human α -**interferon** compns.)

IT **Albumins, biological studies**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (serum, human or bovine; oral **recombinant** human α -**interferon** compns.)

IT Drug delivery systems

(tablets; oral **recombinant** human α -
interferon compns.)

IT **Interferons**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (α , **recombinant** human; oral
recombinant human α -**interferon**
 compns.)

IT **Interferons**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (α -2a, **recombinant** human; oral
recombinant human α -**interferon**
 compns.)

IT **Interferons**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (α -2b, **recombinant** human; oral
recombinant human α -**interferon**
 compns.)

IT **Interferons**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (α 1, **recombinant** human; oral
recombinant human α -**interferon**
 compns.)

IT 61512-21-8, Thymosin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (F5; oral **recombinant** human α -
interferon compns.)

IT 7585-39-9, β -Cyclodextrin 25322-68-3

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (oral **recombinant** human α -**interferon**
 compns.)

L66 ANSWER 15 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1997:756962 HCAPLUS
 DN 128:16442
 ED Entered STN: 04 Dec 1997
 TI Stabilization of **interferons** in aqueous solution for manufacture
 of sublingually administered tablets
 IN Rothschild, Peter R.
 PA Feronpatent Limited, Ire.; Rothschild, Peter R.
 SO PCT Int. Appl., 12 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K038-21
 ICS A61K009-20
 CC 63-6 (Pharmaceuticals)

FAN.CNT 1	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9741885	A1	19971113	WO 1997-IB531	19970509 <--
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU	9724011	A1	19971126	AU 1997-24011	19970509 <--
EP	920329	A1	19990609	EP 1997-919596	19970509 <--
EP	920329	B1	20020925		
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			

AT 224725 E 20021015 AT 1997-919596 19970509 <--
 ES 2184084 T3 20030401 ES 1997-919596 19970509 <--
 PRAI WO 1996-IB433 A 19960509 <--
 WO 1997-IB531 W 19970509 <--
 AB Natural and **recombinant interferons** are stabilized
 with bidistd. water, lactose, **albumin**, sodium mono- and
 dihydrogen phosphates, (C5H10O5)n, such as arabic gum, dissolved and diluted
 in 20 % ethanol solution to the fourth decimal by homeopathic method. The
 final solution is sprayed on to an excipient comprising of 20 % arabic gum,
 30 % lactose and 50 % starch for manufacturing tablets of 100 mg each
 containing 200
 I.U. of human alfa-**interferon**. The tablets are sublingually
 administered to the patient for treatment of viral **infections**
 sensitive to **interferon**. Preparation of sublingual tablets according
 above method is disclosed.
 ST stabilization **interferon** polysaccharide sublingual
 pharmaceutical tablet
 IT Hepatitis
 (B; stabilization of **interferons** in aqueous solution for manufacture of
 sublingually administered tablets)
 IT Hepatitis
 (C; stabilization of **interferons** in aqueous solution for manufacture of
 sublingually administered tablets)
 IT Therapy
 (homeopathy; stabilization of **interferons** in aqueous solution for
 manufacture of sublingually administered tablets)
 IT Antitumor agents
 Stabilizing agents
 (stabilization of **interferons** in aqueous solution for manufacture of
 sublingually administered tablets)
 IT **Albumins, biological studies**
Interferons
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (stabilization of **interferons** in aqueous solution for manufacture of
 sublingually administered tablets)
 IT Drug delivery systems
 (tablets, sublingual; stabilization of **interferons** in aqueous
 solution for manufacture of sublingually administered tablets)
 IT **Infection**
 (viral; stabilization of **interferons** in aqueous solution for manufacture
 of sublingually administered tablets)
 IT **Interferons**
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (α ; stabilization of **interferons** in aqueous solution
 for manufacture of sublingually administered tablets)
 IT **Interferons**
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (β ; stabilization of **interferons** in aqueous solution
 for manufacture of sublingually administered tablets)
 IT **Interferons**
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (γ ; stabilization of **interferons** in aqueous solution for
 manufacture of sublingually administered tablets)
 IT 63-42-3, Lactose 7558-79-4, Sodium monohydrogen phosphate 7558-80-7,
 Sodium dihydrogen phosphate 9000-01-5, Arabic gum 9005-25-8, Starch,
 biological studies
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (stabilization of **interferons** in aqueous solution for manufacture of
 sublingually administered tablets)

ED Entered STN: 28 Oct 1996
 TI Shelf-life of **recombinant** human **interferon** .
alpha.2b under different storage conditions
 AU Barberia, Daisy; Vega, Maribel; Ferrero, Joel; Duany, Lady; Moya, Galina;
 Curras, Tania; Martinez, Maida; Cruz, Astorio; Gil, Miriela; Quintana,
 Marisel
 CS Centro de Ingenieria Genetica y Biotecnologia, Havana, Cuba
 SO Biotecnologia Aplicada (1996), 13(3), 190-194
 CODEN: BTAPEP; ISSN: 0864-4551
 PB Sociedad Iberolatinoamericana de Biotecnologia Aplicada a la Salud
 DT Journal
 LA Spanish
 CC 63-5 (Pharmaceuticals)
 AB The stability test studies under accelerated and normal storage conditions
 carried out with **recombinant** human alpha 2b **interferon**
 (hu-r alpha 2b IFN) in phosphate buffer 0.1M, pH 7.0, with and without
albumin, in order to establish its shelf-life at refrigerating and
 frozen conditions. According to the accelerated study the authors
 concluded that no alterations will interfere with the recognition of hu-r
 alpha 2b IFN in ELISA in at least five years when stored at -70 or
 -20°. Otherwise, when stored at 4°, a loss of 10% may occur
 in one year. The authors corroborated this when the presence of new
 structures which might affect the protein immunol. recognition were
 detected by RP-HPLC. No stabilizing properties of **albumin** on
 hu-r alpha 2b IFN were observed at least when it is in phosphate buffer 0.1M,
 pH 7.0 and under accelerated storing conditions.
 ST **interferon** stability denaturation freezing
 IT **Albumins, biological studies**
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (shelf-life of **recombinant** human **interferon**
 α 2b under different storage conditions)
 IT **Interferons**
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (α -2b, shelf-life of **recombinant**
 human **interferon** α 2b under
 different storage conditions)

L66 ANSWER 17 OF 29 HCPLUS COPYRIGHT 2004 ACS on STN
 AN 1996:43019 HCPLUS
 DN 124:66661
 ED Entered STN: 23 Jan 1996
 TI Stabilized β -**interferon** liquid formulations
 IN Samaritani, Fabrizio; Natale, Patrizia
 PA Applied Research Systems ARS Holding N.V., Neth.
 SO PCT Int. Appl., 17 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K038-21
 CC 63-6 (Pharmaceuticals)

FAN.CNT 1	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9531213	A1	19951123	WO 1995-EP1825	19950515 <--
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2190465	AA	19951123	CA 1995-2190465	19950515 <--
	AU 9526704	A1	19951205	AU 1995-26704	19950515 <--
	AU 704827	B2	19990506		
	EP 759775	A1	19970305	EP 1995-921749	19950515 <--
	EP 759775	B1	20000726		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 10500125	T2	19980106	JP 1995-529360	19950515 <--

AT 194917 E 20000815 AT 1995-921749 19950515 <--
 ES 2148526 T3 20001016 ES 1995-921749 19950515 <--
 PRAI IT 1994-RM300 A 19940516 <--
 WO 1995-EP1825 W 19950515 <--
 AB β -Interferon liquid formulations are stabilized with a polyol, a nonreducing sugar, or an amino acid. In particular, the formulations are stabilized with a polyol, such as mannitol. The formulations, preferably, furthermore comprise a buffer, such as acetate buffer at a pH 3-4 and human albumin at a min. quantity. The β -interferon is preferably recombinant.
 ST interferon soln stabilizer polyol albumin buffer;
 mannitol albumin acetate buffer interferon stability
 IT Buffer substances and systems
 (acetate; stabilized β -interferon liquid
 formulations)
 IT **Albumins, biological studies**
 Amino acids, biological studies
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (stabilized β -interferon liquid formulations)
 IT Carbohydrates and Sugars, biological studies
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (nonreducing, stabilized β -interferon liquid
 formulations)
 IT Alcohols, biological studies
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (polyhydric, stabilized β -interferon liquid
 formulations)
 IT Pharmaceutical dosage forms
 (solns., stabilized β -interferon liquid
 formulations)
 IT **Interferons**
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (β , recombinant; stabilized β -
 interferon liquid formulations)
 IT 56-40-6, Glycine, biological studies 57-50-1, Saccharose, biological
 studies 69-65-8, D-Mannitol
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (stabilized β -interferon liquid formulations)

L66 ANSWER 18 OF 29 HCPLUS COPYRIGHT 2004 ACS on STN
 AN 1995:498838 HCPLUS
 DN 122:248213
 ED Entered STN: 20 Apr 1995
 TI Influence of human serum albumin content in
 formulations on the bioequivalency of interferon alfa-2a given
 by subcutaneous injection in healthy male volunteers
 AU Zhi, Jianguo; Teller, Stuart B.; Satoh, Hiroko; Koss-Twardy, Susan G.;
 Luke, David R.
 CS Department of Clinical Pharmacokinetics, Hoffmann-La Roche, Inc., Nutley,
 NJ, 07110-1199, USA
 SO Journal of Clinical Pharmacology (1995), 35(3), 281-4
 CODEN: JCPCBR; ISSN: 0091-2700
 DT Journal
 LA English
 CC 63-6 (Pharmaceuticals)
 Section cross-reference(s): 1
 AB To determine the influence of human serum albumin (HSA)
 content in formulations on the bioequivalency of recombinant
 interferon α 2a, a double-blind, randomized,
 two-way crossover study was conducted in 24 healthy male volunteers.
 Subjects received a single s.c. injection of 18 million IU of Roferon-A
 reconstituted with either the diluent containing 10 mg of HSA or the HSA-free
 diluent; final HSA contents in the 2 formulations were 15 and 5 mg, resp.

Administration of the 2 formulations resulted in similar 48-h Roferon-A serum concentration-time profiles and comparable frequency and intensity of adverse events. The statistical anal. using the two one-sided tests procedure showed that both formulations were bioequivalent for pharmacokinetic parameters such as Cmax, tmax, AUC48, and AUC. Thus, a threefold change in HSA content in formulations does not alter the bioequivalency of Roferon-A.

ST **interferon** bioavailability bioequivalence injection

albumin

IT Drug bioavailability
(human serum **albumin** effect on bioequivalence of
recombinant interferon α 2a from s.c.
injection in humans)

IT **Albumins, biological studies**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human serum **albumin** effect on bioequivalence of
recombinant interferon α 2a from s.c.
injection in humans)

IT Pharmaceutical dosage forms

(injections, s.c., human serum **albumin** effect on
bioequivalence of **recombinant interferon**
 α 2a from s.c. injection in humans)

IT **Interferons**

RL: BPR (Biological process); BSU (Biological study, unclassified); THU
(Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(α -2a, human serum **albumin** effect
on bioequivalence of **recombinant interferon**
 α 2a from s.c. injection in humans)

L66 ANSWER 19 OF 29 HCPLUS COPYRIGHT 2004 ACS on STN

AN 1994:6892 HCPLUS

DN 120:6892

ED Entered STN: 08 Jan 1994

TI Novel **recombinant** human **IFN- β** , its preparation, and pharmaceutical compositions containing it

IN Siklosi, Thomas; Joester, Karl-eduard; Hofer, Hans

PA BIOFERON Biochemische Substanzen GmbH und Co, Germany

SO Eur. Pat. Appl., 19 pp.

CODEN: EPXXDW

DT Patent

LA German

IC ICM C07K015-26

ICS C07K003-28; A61K037-66

CC 16-2 (Fermentation and Bioindustrial Chemistry)

Section cross-reference(s): 15

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 529300	A1	19930303	EP 1992-112427	19920721 <--
	EP 529300	B1	19981014		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE				
	DE 4128319	A1	19930304	DE 1991-4128319	19910827 <--
	AT 172206	E	19981015	AT 1992-112427	19920721 <--
	ES 2121804	T3	19981216	ES 1992-112427	19920721 <--
PRAI	DE 1991-4128319		19910827 <--		
AB	A recombinant human β - interferon (IFN-β) produced in mammalian cells, whose oligosaccharide component comprises biantennary $\geq 60\%$, triantennary $\geq 15\%$, and tetraantennary 0-5% and contains fucose and $\geq 80\%$ sialic acid, is useful for treatment of tumors, especially Kaposi's sarcoma. Thus, recombinant IFN-β was produced in transfected CHO BIC 8622 cells in MEM containing fetal calf serum and secreted into the medium in a yield of 1 + 105-1 + 106 IU/L. The				

IFN- β was purified by liquid-liquid extraction in a PEG 2000-salt solution system, affinity chromatog. on Blue Dextran FF, metal chelate chromatog. on a Zn²⁺-loaded chelating Sepharose column, and size exclusion chromatog. on Sephadryl. The product showed a purity of >99% and high stability at -20, +15, or +25° when mixed with buffered human serum **albumin** and stored for 1-4 wk. Enzymic removal of terminal sialic acid residues diminished the stability.

- ST **recombinant beta interferon** purifn
- IT Polyoxalkylenes, biological studies
- Salts, biological studies
- RL: BIOL (Biological study)
 - (in β -**interferon** purification, by partition)
- IT Oligosaccharides
- Sialic acids
- RL: BIOL (Biological study)
 - (of **recombinant β -interferon**)
- IT Chromatography, gel
 - (of β -**interferon**)
- IT Partition
 - (of β -**interferon**, in polyalkylene glycol/dextran and polyalkylene glycol/salt systems)
- IT Neoplasm inhibitors
 - (**recombinant β -interferon**)
- IT Dyes
 - (β -**interferon** affinity chromatog. on)
- IT Animal cell line
 - (CHO, **recombinant β -interferon** manufacture with)
- IT Neoplasm inhibitors
 - (Kaposi's sarcoma, **recombinant β -interferon** as)
- IT Chromatography, column and liquid
 - (affinity, of β -**interferon**, on dye)
- IT Coordination compounds
 - RL: BIOL (Biological study)
 - (chelates, stationary phases containing, for β -**interferon** chromatog.)
- IT **Interferons**
 - RL: BIOL (Biological study)
 - (β , purification of **recombinant**, for Kaposi's sarcoma treatment)
- IT 12236-82-7 148498-83-3, Blue Sepharose FF 57-55-6, 1,2-Propanediol, uses 107-21-1, 1,2-Ethanediol, uses
 - RL: BIOL (Biological study)
 - (in β -**interferon** purification, by affinity chromatog.)
- IT 56-40-6, Glycine, uses 71-00-1, Histidine, uses 288-32-4, Imidazole, uses
 - RL: USES (Uses)
 - (in β -**interferon** purification, by metal chelate chromatog.)
- IT 62-76-0, Sodium oxalate 68-04-2, Sodium citrate 25322-68-3, Polyethylene glycol 25322-69-4, Polypropylene glycol 7447-40-7, Potassium chloride (KCl), uses 7447-41-8, Lithium chloride, uses 7558-79-4, Disodium phosphate 7558-80-7, Sodium dihydrogen phosphate 7647-14-5, Sodium chloride, uses 7681-11-0, Potassium iodide, uses 7681-82-5, Sodium iodide, uses 7757-82-6, Sodium sulfate, uses 7758-11-4, Dipotassium phosphate 7778-80-5, Potassium sulfate, uses 7783-20-2, Ammonium sulfate, uses 9004-54-0, Dextran, uses 12125-02-9, Ammonium chloride, uses
 - RL: BIOL (Biological study)
 - (in β -**interferon** purification, by partition)
- IT 131-48-6, N-Acetylneuraminic acid 1113-83-3 2438-80-4, Fucose

32181-59-2, N-Acetyllactosamine 78392-81-1 83412-55-9 84813-89-8
123618-73-5 131432-29-6 148553-76-8 148553-77-9 148553-78-0
148553-79-1 148553-80-4 148553-81-5 148614-65-7 148615-15-0
RL: BIOL (Biological study)
(of **recombinant β -interferon**)
IT 7440-02-0D, Nickel, chelates 7440-48-4D, Cobalt, chelates 7440-50-8D,
Copper, chelates 7440-66-6D, Zinc, chelates 12774-36-6, Sephadex G150
97599-42-3, Superose 12 119332-87-5, Sephadryl S 200 High Resolution
148499-25-6, TSK-SW 3000
RL: BIOL (Biological study)
(**β -interferon** purification by chromatog. on)

L66 ANSWER 20 OF 29 HCPLUS COPYRIGHT 2004 ACS on STN
AN 1992:468225 HCPLUS
DN 117:68225
ED Entered STN: 23 Aug 1992
TI Human **β -interferon** incubated with muscle
homogenate is protected by **albumin** but not by proteinase
inhibitors
AU Paulesu, L.; Pessina, G. P.; Bocci, V.
CS Inst. Gen. Physiol., Univ. Siena, Siena, 53100, Italy
SO Proceedings of the Society for Experimental Biology and Medicine (1992), 200(3), 414-17
CODEN: PSEBAA; ISSN: 0037-9727
DT Journal
LA English
CC 15-5 (Immunochemistry)
Section cross-reference(s): 1
AB The scarce bioavailability of **β -interferon** (**IFN-β**) after i.m. administration is probably due
either to the binding of **IFN-β** to the
interstitial matrix, or to lymphatic absorption and/or to local breakdown
by lysosomal proteinases from muscle. In this work, the authors first
showed that after i.m. injection, the apparent bioavailability of natural
human **IFN-β** is about 10% of that of
recombinant IFN-α 2 and then they
evaluated the effects of proteinase inhibitors and **albumin** on
IFN-β incubated at 37° with muscle
homogenate. IFN biol. activity decreased spontaneously by about 20% after
incubation for 6 h at 37° in Hanks' solution, but it was almost
completely lost after incubation with muscle homogenate. Proteinase
inhibitors (α 1-antitrypsin, α 2-macroglobulin, aprotinin,
soybean trypsin inhibitor, leupeptin, EP-459, and EP-475) failed to block
the inactivation of **IFN-β** by muscle proteinases,
whereas **albumin** exerted a partial but consistent protection.
ST **interferon beta** bioavailability muscle **albumin**
; proteinase inhibitor **interferon beta** bioavailability
IT Muscle, metabolism
(**interferon-β** of humans inactivation by,
albumin and proteinase inhibitors effect on)
IT **Albumins, biological studies**
RL: BIOL (Biological study)
(muscle inactivation of human **interferon-β**
inhibition by)
IT **Interferons**
RL: BIOL (Biological study)
(β , muscle inactivation of human, **albumin** and
proteinase inhibitors effect on)
IT 138674-34-7, Cysteine proteinase inhibitor 139691-92-2, Serine
proteinase inhibitor
RL: BIOL (Biological study)
(muscle inactivation of human **interferon-β**
response to)

L66 ANSWER 21 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1991:478932 HCAPLUS
 DN 115:78932
 ED Entered STN: 23 Aug 1991
 TI Stable formulations of lipophilic **recombinant** proteins
 IN Fernandes, Peter M.; Taforo, Terrance
 PA Cetus Corp., USA
 SO U.S., 20 pp. Cont.-in-part of U.S. Ser. No. 752,403.
 CODEN: USXXAM
 DT Patent
 LA English
 IC ICM A61K037-02
 ICS A61K045-02
 NCL 424085200
 CC 63-6 (Pharmaceuticals)
 Section cross-reference(s): 16
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4992271	A	19910212	US 1985-775751	19850913 <--
	US 4462940	A	19840731	US 1983-495896	19830518 <--
	CA 1339707	A1	19980310	CA 1986-516417	19860820 <--
	AU 8662642	A1	19870319	AU 1986-62642	19860912 <--
	AU 590896	B2	19891123		
	EP 215658	A2	19870325	EP 1986-307070	19860912 <--
	EP 215658	A3	19890208		
	EP 215658	B1	19940601		
	R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
	AT 106247	E	19940615	AT 1986-307070	19860912 <--
	JP 62067032	A2	19870326	JP 1986-215063	19860913 <--
	JP 06004542	B4	19940119		
	US 5643566	A	19970701	US 1995-474769	19950607 <--
PRAI	US 1982-422421		19820923	<--	
	US 1983-495896		19830518	<--	
	US 1984-592077		19840323	<--	
	US 1985-752403		19850705	<--	
	US 1985-775751		19850913	<--	
	EP 1986-307070		19860912	<--	
	US 1986-923425		19861027	<--	
	US 1992-865411		19920507	<--	
	US 1994-266832		19940628	<--	
AB	An improved process for recovering and purifying lipophilic recombinant proteins such as human β - interferon and interleukin-2 (IL-2) from their hosts yields a protein preparation which is formulated into a stable pharmaceutical composition having a therapeutically effective amount of the biol. active recombinant lipophilic protein dissolved in a nontoxic, inert, therapeutically compatible aqueous based carrier medium at a pH of 6.8 to 7.8. The medium also contains a stabilizer for the protein, such as human serum albumin and human plasma protein fraction. IL-2 produced by recombinant Escherichia coli was purified by a series of steps and formulated with human serum albumin (final concentration 2.5%) at pH 2.58.				
ST	interleukin Escherichia albumin stabilizer; interferon recombinant albumin formulation				
IT	Escherichia coli (beta-interferons and interleukin 2 from)				
IT	Proteins, biological studies				
	RL: BIOL (Biological study) (of blood plasma, as stabilizers for recombinant interleukin 2-containing pharmaceutical compns.)				

- IT Pharmaceutical dosage forms
 (of **recombinant β -interferons** and
 interleukin 2, stabilizers in, **albumins** and sugars as)
- IT **Albumins, biological studies**
 RL: BIOL (Biological study)
 (stabilizers, for **recombinant** interleukin 2-containing
 pharmaceutical compns.)
- IT Lymphokines and Cytokines
 RL: BIOL (Biological study)
 (interleukin 2, **recombinant**, from Escherichia coli,
 stabilized formulations of, **albumins** and sugars in)
- IT **Interferons**
 RL: BIOL (Biological study)
 (β , **recombinant**, from Escherichia coli,
 stabilized formulations of, **albumins** and sugars in)
- IT 69-65-8, Mannitol
 RL: BIOL (Biological study)
 (stabilizer, for **recombinant** interleukin-2 containing
 pharmaceutical composition)
- IT 50-99-7, Dextrose, biological studies
 RL: BIOL (Biological study)
 (stabilizer, for **recombinant β -**
interferon-containing pharmaceutical composition)
- L66 ANSWER 22 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1990:153049 HCAPLUS
 DN 112:153049
 ED Entered STN: 28 Apr 1990
 TI Use of human serum **albumin** signal peptide in **recombinant**
 protein manufacture and secretion with yeast
 IN Hayasuke, Naofumi; Nakagawa, Yukimitsu; Ishida, Yutaka; Okabayashi, Ken;
 Murakami, Kohji; Tsutsui, Kiyoshi; Ikegaya, Kazuo; Minamino, Hitoshi;
 Ueda, Sadao; et al.
 PA Green Cross Corp., Japan
 SO Eur. Pat. Appl., 35 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 IC ICM C12N015-00
 ICS C12P021-00
 CC 3-4 (Biochemical Genetics)
- FAN.CNT 1
- | | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|--------------|
| PI | EP 319641 | A1 | 19890614 | EP 1988-107087 | 19880503 <-- |
| | EP 319641 | B1 | 19930922 | | |
| | R: BE, CH, DE, ES, FR, GB, IT, LI, NL, SE | | | | |
| | JP 02167095 | A2 | 19900627 | JP 1988-103339 | 19880426 <-- |
| | JP 2791418 | B2 | 19980827 | | |
| | CA 1326217 | A1 | 19940118 | CA 1988-565766 | 19880503 <-- |
| | ES 2059428 | T3 | 19941116 | ES 1988-107087 | 19880503 <-- |
| | KR 9705250 | B1 | 19970414 | KR 1988-5553 | 19880513 <-- |
| | US 5503993 | A | 19960402 | US 1995-445783 | 19950522 <-- |
| PRAI | JP 1987-306674 | A | 19871202 | <-- | |
| | JP 1988-45605 | A | 19880226 | <-- | |
| | US 1988-190553 | B1 | 19880505 | <-- | |
| | US 1992-913785 | B1 | 19920630 | <-- | |
| OS | MARPAT 112:153049 | | | | |
| AB | A method for producing and secreting proteins with yeast comprises transformation of the yeast with a chimeric gene for a human albumin signal peptide and the coding sequence for the desired protein and expression of the gene. Plasmid pNH008, containing the GAL1 promoter linked to a synthetic human serum albumin signal | | | | |

sequence **fused** to the mature human serum **albumin** gene and the pho5 terminator, was constructed. *Saccharomyces cerevisiae* AH22 transformed with this plasmid produced 160 mg **albumin**/L culture medium after 48 h incubation.

ST protein secretion yeast **albumin** signal peptide; *Saccharomyces* human **albumin** manuf secretion

IT *Saccharomyces cerevisiae*
(human serum **albumin** manufacture and secretion with, **albumin** signal peptide in)

IT Molecular cloning
(in yeast, human serum **albumin** signal sequence in)

IT **Albumins, preparation**
RL: PREP (Preparation)
(manufacture of, of human, with yeast, human serum **albumin** signal peptide in)

IT Lymphokines and Cytokines
RL: PROC (Process)
(manufacture of, with yeast, human serum **albumin** signal peptide in)

IT Protein sequences
(of **albumin** signal peptide analogs, of human)

IT Yeast
(**recombinant** protein secretion from, signal peptide of human serum **albumin** in)

IT Deoxyribonucleic acid sequences
(**albumin**-specifying, signal peptide analog, of human)

IT Gene and Genetic element
RL: BIOL (Biological study)
(**chimeric**, for signal sequence of human serum **albumin** and desired protein, expression in yeast of, protein secretion in relation to)

IT Plasmid and Episome
(pNH008, **chimeric** human serum **albumin** signal peptide-**albumin** gene on, expression in *Saccharomyces cerevisiae* of, **albumin** secretion in relation to)

IT Peptides, biological studies
RL: BIOL (Biological study)
(signal, of human serum **albumin**, protein secretion from **recombinant** yeast using)

IT Gene and Genetic element, animal
(signal sequence, of human serum **albumin** gene, protein secretion from yeast in relation to)

IT **Interferons**
RL: PROC (Process)
(α , manufacture of, with yeast, human serum **albumin** signal peptide in)

IT **Interferons**
RL: PROC (Process)
(β , manufacture of, with yeast, human serum **albumin** signal peptide in)

IT **Interferons**
RL: PROC (Process)
(γ , manufacture of, with yeast, human serum **albumin** signal peptide in)

IT 125677-90-9P 125677-91-0P 125677-92-1P 125677-93-2P 125677-94-3P
125677-95-4P
RL: PREP (Preparation)
(human serum **albumin** signal peptide derivative, **recombinant** protein manufacture and secretion with yeast in relation to)

IT 125677-89-6P
RL: PREP (Preparation)
(human serum **albumin** signal peptide, **recombinant**)

protein manufacture and secretion with yeast in relation to)
 IT 9001-27-8P, Factor VIII 9002-72-6P, Growth hormone 9004-10-8P,
 Insulin, biological studies 9039-53-6P, Urokinase 11096-26-7P,
 Erythropoietin 62683-29-8P, Colony-stimulating factor 85637-73-6P,
 Atriopeptin
 RL: IMF (Industrial manufacture); PREP (Preparation)
 (manufacture and secretion of, with yeast, human serum **albumin**
 signal peptide in relation to)
 IT 126115-99-9P
 RL: PREP (Preparation)
 (nucleotide sequence encoding human serum **albumin** signal
 peptide, **recombinant** protein manufacture and secretion with yeast
 in relation to)

L66 ANSWER 23 OF 29 HCPLUS COPYRIGHT 2004 ACS on STN
 AN 1989:639534 HCPLUS
 DN 111:239534
 ED Entered STN: 23 Dec 1989
 TI Pharmaceutical compositions containing **recombinant**
interferon-β
 IN Taforo, Terrance; Thomson, Jody; Shaked, Ze'ev; Hershenson, Susan;
 Thomson, James W.; Stewart, Tracy
 PA Cetus Corp., USA
 SO PCT Int. Appl., 80 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K047-00
 ICS A61K045-02
 CC 63-6 (Pharmaceuticals)
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8902750	A1	19890406	WO 1988-US3313	19880926 <--
	W: AU, DK, JP, NO				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	US 5183746	A	19930202	US 1987-100679	19870929 <--
	AU 8825351	A1	19890418	AU 1988-25351	19880926 <--
PRAI	US 1987-100679		19870929 <--		
	US 1986-923423		19861027 <--		
	WO 1988-US3313		19880926 <--		
AB	A stable parenteral composition in liquid or lyophilized form comprises a recombinant interferon-β (IFN-β) . beta. protein dissolved in an inert carrier medium containing nonionic polymeric surfactants as a solubilizer/stabilizer. The surfactants include polyoxyethylene sorbitan fatty acid esters, a mixture of ethoxylated fatty alc. ethers and lauryl ether, ethoxylated octylphenol, a mixture of ethoxylated or propoxylated alc., polyethylene glycol monooleate, ethoxylated phenol, and propylene oxide-ethylene oxide block copolymers. The composition further comprises addnl. bulking/stabilizing agents, such as dextrose. An IFN-β analog designated as IFN-β ser17 was recovered from Escherichia coli culture media and stabilized by adding 0.15% Trycol LAL-12 and pH was adjusted to 7.0 with NaOH. A bulking/stabilizing agent, i.e., 5% dextrose, was then added and the solution was sterile-filtered, aseptically filled into vials, and lyophilized. The IFN-β formulations of this invention contain very low levels of aggregates and other potentially immunogenic characterisitcs and minimal or no strong solubilizing agents, such as SDS, and they are nontoxic and have good shelf life.				
ST	interferon beta surfactant solubilizer injection; lyophilization interferon beta stability				
IT	Solubilizers				

Stabilizing agents
 (nonionic surfactants and sugars as, for **interferon**
 β -containing parenteral compns.)

IT **Albumins, biological studies**

RL: BIOL (Biological study)
 (parenteral **interferon- β** composition containing
 nonionic surfactants and, as stabilizer)

IT Carbohydrates and Sugars, biological studies

RL: BIOL (Biological study)
 (parenteral **interferon- β** composition containing
 nonionic surfactants and, as stabilizers)

IT Surfactants
 (nonionic, parenteral **interferon- β** composition
 containing, as stabilizers)

IT Pharmaceutical dosage forms
 (parenterals, containing β -**interferons**, nonionic
 surfactants and sugars in, as solubilizers/stabilizers)

IT **Interferons**

RL: BIOL (Biological study)
 (β , parenteral compns. containing, solubilizers/stabilizers
 for, nonionic surfactants and sugars as)

IT 50-70-4, Sorbitol, biological studies 50-99-7, Dextrose, biological
 studies 56-81-5, Glycerol, biological studies 69-65-8, Mannitol
 87-89-8, Inositol 151-21-3, Sodium dodecyl sulfate, biological studies

RL: BIOL (Biological study)
 (parenteral **interferon- β** composition containing
 nonionic surfactants and, as stabilizer)

IT 9002-92-0, Ethoxylated lauryl alcohol 9002-93-1, Triton X305
 9004-78-8, Ethoxylated phenol 9004-96-0 9005-64-5, Polyoxyethylene
 sorbitan monolaurate 9005-65-6 9036-19-5, Ethoxylated octylphenol
 12616-49-8, Plurafac C17 106392-12-5, Propylene oxide-ethylene oxide
 blocker copolymer

RL: BIOL (Biological study)
 (parenteral **interferon- β** composition containing, as
 stabilizer)

L66 ANSWER 24 OF 29 HCPLUS COPYRIGHT 2004 ACS on STN

AN 1989:18548 HCPLUS

DN 110:18548

ED Entered STN: 21 Jan 1989

TI Method for treatment of essential (hemorrhagic) thrombocythemia with human
 α -**interferon**

IN Delwiche, Francis; Flament-Grivegnee, Jocelyn; Gangji, Diamond; Monsieur,
 Rita; Stryckmans, Pierre; Velu, Thierry; Wybran, Joseph

PA Boehringer Ingelheim International G.m.b.H., Fed. Rep. Ger.

SO U.S., 4 pp.

CODEN: USXXAM

DT Patent

LA English

IC ICM A61K045-02

NCL 424085000

CC 1-8 (Pharmacology)

Section cross-reference(s): 63

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	-----	-----	-----	-----

PI US 4743445 A 19880510 US 1985-758729 19850725 <--

PRAI US 1985-758729 19850725 <--

AB Essential thrombocythemia is treated by administration of an effective

amount of human α -**interferon**. Patients with

essential thrombocythemia were given i.m. injections of 5 + 106 IU

recombinant human interferon- α 2(Arg)

(I)/day for 30 days. After 15 days, the dose was doubled if the results

(I)/day for 30 days. After 15 days, the dose was doubled if the results

of the treatment were insufficient. After 30 days, the same dose was given twice a week as a maintenance dose. In all patients the number of thrombocytes returned to normal. A parenteral formulation comprises I 5 + 106 IU, isotonic phosphate buffer (pH 7) q.s., human serum **albumin** 20.0 mg, and water for injection 1.0 mL.

- ST essential thrombocythemia **alpha interferon**
 IT Blood platelet
 (α -**interferon** of human effect on)
 IT Blood platelet
 (disease, essential thrombocythemia, treatment of, with α -**interferon** of human)
 IT **Interferons**
 RL: BIOL (Biological study)
 (α , essential thrombocythemia treatment with, of human)
 IT 118104-04-4
 RL: BIOL (Biological study)
 (essential thrombocythemia treatment with)

- L66 ANSWER 25 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1988:562850 HCAPLUS
 DN 109:162850
 ED Entered STN: 12 Nov 1988
 TI **Recombinant human interferon alpha-2a:**
 delivery to lymphoid tissue by selected modes of application
 AU Supersaxo, Andreas; Hein, Wayne; Gallati, Harald; Steffen, Hans
 CS Preclin. Dev., F. Hoffmann-La Roche und Co. Ltd., Basel, Switz.
 SO Pharmaceutical Research (1988), 5(8), 472-6
 CODEN: PHREEB; ISSN: 0724-8741
 DT Journal
 LA English
 CC 1-2 (Pharmacology)
 AB Following s.c. or injection device (i.d.) administration,
 recombinant human interferon α -2a (rIFN
 α -2a) of mol. weight 19,000 was absorbed mainly by the lymphatics.
 This results in high rIFN α -2a levels in the lymphoid tissue which
 drains the application site, while blood plasma levels are relatively low.
 The maximum measured concns. of rIFN α -2a in the efferent popliteal
 lymph varied by a factor of 105 between intradermal/s.c. and i.v.
 administration and was affected neither by the **infusion** rate nor
 by the coadministration of **albumin**. This may help to improve
 the mode of administration and therapeutic efficacy of protein drugs whose
 targets are lymphoid cells.
 ST **interferon α 2a delivery lymph gland**
 IT Lymphatic system
 (**interferon α -2a absorption by, after**
 parenteral administrations)
 IT **Albumins, biological studies**
 RL: BIOL (Biological study)
 (**interferon α -2a delivery to lymphoid tissue**
 in relation to)
 IT Lymph gland
 (**interferon α -2a delivery to, parenteral**
 administration routes for)
 IT **Interferons**
 RL: BIOL (Biological study)
 (α -2a, delivery to lymphoid tissue of
 recombinant, parenteral administration routes for)

- L66 ANSWER 26 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1987:583557 HCAPLUS
 DN 107:183557
 ED Entered STN: 14 Nov 1987
 TI Improved formulation for **recombinant β -**

interferon with protein or sugar stabilizer
 IN Hanisch, Wolfgang Helmut; Taforo, Terrance; Fernandes, Peter Michael
 PA Cetus Corp., USA
 SO Eur. Pat. Appl., 34 pp.
 CODEN: EPXXDW

DT Patent
 LA English
 IC ICM A61K045-02
 ICS A61K047-00; C07K003-02; C12P021-02
 CC 63-6 (Pharmaceuticals)
 Section cross-reference(s): 3

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 215658	A2	19870325	EP 1986-307070	19860912 <--
	EP 215658	A3	19890208		
	EP 215658	B1	19940601		
	R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
	US 4992271	A	19910212	US 1985-775751	19850913 <--
	AT 106247	E	19940615	AT 1986-307070	19860912 <--
PRAI	US 1985-775751		19850913 <--		
	US 1982-422421		19820923 <--		
	US 1983-495896		19830518 <--		
	US 1984-592077		19840323 <--		
	US 1985-752403		19850705 <--		
	EP 1986-307070		19860912 <--		

AB **Recombinant β-human interferon (.beta**
 .-HIFN) is dissolved in a non-toxic, inert, therapeutically compatible aqueous carrier, at a pH of 2-4. The solution contains a stabilizer for the β-HIFN, particularly human plasma protein fraction, human serum albumin, or mannitol. This formulation results in very low sodium dodecyl sulfate levels. β -**Interferon** 0.25 mg/mL was formulated using 2.5% plasma protein fraction at pH 3-4, incubated 15-45 min.; the pH was adjusted to 7.3-7.5. At this pH, the solns. were very clear. The use of 5.0% human serum albumin also gave clear solns., whereas 2.5% HSA resulted in slightly hazy solns.

ST **interferon** formulation protein solubilization; stabilizer

recombinant beta interferon

IT **Albumins, biological studies**RL: BIOL (Biological study)
 (human, stabilizer for **recombinant β-human interferon**)

IT Proteins, specific or class, biological studies

RL: BIOL (Biological study)
 (of blood plasma, as stabilizer for **recombinant β-human interferon**)IT **Recombination, genetic**
 (of β -**interferon**, purification and formulation for)IT **Interferons**
 (β -, recombinant, stabilization of, in formulation)

IT 151-21-3, Sodium dodecyl sulfate, biological studies

RL: PRP (Properties)
 (reduced levels of, in formulations of β -**interferon**)IT 50-99-7, Dextrose, biological studies 69-65-8, Mannitol
 RL: BIOL (Biological study)
 (stabilizer, for **recombinant β - interferon**-containing pharmaceutical composition)

L66 ANSWER 27 OF 29 HCPLUS COPYRIGHT 2004 ACS on STN
 AN 1987:464710 HCPLUS
 DN 107:64710

ED Entered STN: 21 Aug 1987
 TI Potency stability of **recombinant** (serine-17) human
interferon- β
 AU Geigert, John; Ziegler, Diana L.; Panschar, Barbara M.; Creasey, Abla A.;
 Vitt, Charles R.
 CS Dep. Tech. Dev., Cetus Corp., Emeryville, CA, 94608, USA
 SO Journal of Interferon Research (1987), 7(2), 203-11
 CODEN: JIREDJ; ISSN: 0197-8357
 DT Journal
 LA English
 CC 63-3 (Pharmaceuticals)
 AB The antiviral activity of Escherichia coli-derived (serine-17) human
interferon- β , formulated with human serum
albumin, is stable for 2 yr when lyophilized and stored under
 refrigeration. This product shows an Arrhenius line fit for the stability
 of its activity when tested at multiple isothermal temps. (25-80°).
 In both isothermal and non-isothermal elevated temperature studies, increasing
 the level of human serum **albumin** in the formulation results in
 increased thermal stability.
 ST **interferon** serine 17 **recombinant** formulation stability
 IT Kinetics of decomposition
 (of **recombinant** human β -**interferon**
 in **albumin** formulation)
 IT **Albumins, uses and miscellaneous**
 RL: USES (Uses)
 (β -**interferon** **recombinant** serine-17
 stabilization by formulation with human)
 IT **Interferons**
 (β -, stability of **recombinant** serine-17, in
 human serum **albumin** formulation)

L66 ANSWER 28 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1986:174635 HCAPLUS
 DN 104:174635
 ED Entered STN: 17 May 1986
 TI **Interferon** solubilization with amino acids
 IN Kato, Yasuki; Hayakawa, Eiji; Furuya, Kunitoshi; Kondo, Akira
 PA Kyowa Hakko Kogyo Co., Ltd., Japan
 SO Eur. Pat. Appl., 14 pp.
 CODEN: EPXXDW

DT Patent
 LA English
 IC ICM A61K045-02
 CC 63-3 (Pharmaceuticals)
 Section cross-reference(s): 15

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 163111	A2	19851204	EP 1985-104849	19850422 <--
	EP 163111	A3	19870930		
	EP 163111	B1	19901003		
	R: DE, FR, GB, IT				
	JP 60243028	A2	19851203	JP 1984-86972	19840428 <--
	JP 05058000	B4	19930825		
	CA 1264665	A1	19900123	CA 1985-479841	19850423 <--
	US 4675183	A	19870623	US 1985-726971	19850425 <--
PRAI	JP 1984-86972		19840428 <--		

AB **Interferon** is solubilized by addition of 5 + 10-6 - 5 +
 10-3 mol amino acid/106 units **interferon**. The amino acid may be
 arginine, histidine, lysine, hydroxylysine, ornithine, glutamine,
 γ -aminobutyric acid, α -aminocaproic acid, or a salt of these
 compds. Thus, 5 mg serum **albumin**, 5 mg NaCl, 30 mg
 arginine-HCl, and 3 + 106 units of γ - **interferon** were

mixed with 2 mL H₂O, and freeze-dried. The product was dissolved in 5 mL H₂O, held 6 h at 25°, and the absorbance was measured at 400 nm.

The amount of γ - **interferon** that remained in solution was 98%. This solubilization may be used to facilitate the isolation and purification of **interferon** produced by recombinant DNA technol.

ST **interferon** solubilizer amino acid; arginine **interferon**
 IT solubilization
 IT Solubilizers
 (amino acids, for **interferon**)
 IT Amino acids, uses and miscellaneous
 RL: PRP (Properties)
 (**interferons** solubilization by)
 IT **Interferons**
 (α -, solubilization of, with amino acids)
 IT **Interferons**
 (β -, solubilization of, with amino acids)
 IT **Interferons**
 (γ -, solubilization of, with amino acids)
 IT 56-85-9, properties 56-87-1, properties 60-32-2 70-26-8 71-00-1,
 properties 74-79-3, properties 657-27-2 1119-34-2 1190-94-9
 2835-81-6 60259-81-6
 RL: PRP (Properties)
 (**interferons** solubilization by)

L66 ANSWER 29 OF 29 HCPLUS COPYRIGHT 2004 ACS on STN
 AN 1986:86802 HCPLUS
 DN 104:86802
 ED Entered STN: 22 Mar 1986
 TI The lymphatic route - II. Pharmacokinetics of human recombinant **interferon- α** 2 injected with **albumin** as a retarder in rabbits
 AU Bocci, Velio; Muscettola, Michela; Naldini, Antonella; Bianchi, Enrica;
 Segre, Giorgio
 CS Inst. Gen. Physiol., Univ. Siena, Siena, 53100, Italy
 SO General Pharmacology (1986), 17(1), 93-6
 CODEN: GEPHDP; ISSN: 0306-3623
 DT Journal
 LA English
 CC 15-5 (Immunoochemistry)
 AB An investigation was conducted to define whether multisite s.c. administration in unanesthetized, unrestrained rabbits of human recombinant **interferon- α** 2 (rec. **IFN- α** 2) either in saline, human **albumin** (ALB) solution (4, 7, and 10% final concns.), or in a solution containing 75 units of hyaluronidase, modified the pharmacokinetic parameters calculated from the IFN plasma level. Plasma disappearance rates of rec. **IFN- α** 2 were measured in rabbits after i.v. administration and the kinetics was adequately represented by a 3-compartment mammillary model. This model was the basis for evaluating the absorption and distribution of rec. **IFN- α** 2 after s.c. administration. The increase of ALB concentration (from 4 to 10%) caused a significant reduction of the plasma IFN maximum clearance, while both the mean residence time and the release time of IFN increased linearly with the ALB concentration. The data support the postulation that s.c. administration of **albumin** acts as an interstitial fluid expander and may favor absorption of IFN via lymphatics rather than blood capillaries. Improvement of therapeutic index of IFN by using this route remains to be shown in clin. trials.
 ST **interferon alpha** pharmacokinetics **albumin**
 IT Lymphatic system
 (**albumin** effect on recombinant $\alpha 2$ -
 interferon pharmacokinetics in relation to, of humans and laboratory

IT animals)
 IT Blood plasma
 (α2- **interferon** pharmacokinetics in, **albumin**
 effect on, in humans and laboratory animals)
 IT **Albumins**
 RL: BIOL (Biological study)
 (α2- **interferon** pharmacokinetics response to, of humans
 and laboratory animals)
 IT **Interferons**
 RL: BIOL (Biological study)
 (α 2-, pharmacokinetics of **recombinant**
 , **albumin** effect on, of humans and laboratory animals)

=> => fil wpix
 FILE 'WPIX' ENTERED AT 16:25:05 ON 02 FEB 2004
 COPYRIGHT (C) 2004 THOMSON DERWENT

FILE LAST UPDATED: 28 JAN 2004 <20040128/UP>
 MOST RECENT DERWENT UPDATE: 200407 <200407/DW>
 DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> NEW WEEKLY SDI FREQUENCY AVAILABLE --> see NEWS <<<
 >>> SLART (Simultaneous Left and Right Truncation) is now
 available in the /ABEX field. An additional search field
 /BIX is also provided which comprises both /BI and /ABEX <<<
 >>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<
 >>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
 PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<
 >>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
 <http://thomsonderwent.com/coverage/latestupdates/> <<<
 >>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
 GUIDES, PLEASE VISIT:
 <http://thomsonderwent.com/support/userguides/> <<<
 >>> ADDITIONAL POLYMER INDEXING CODES WILL BE IMPLEMENTED FROM
 DERWENT UPDATE 200403.
 THE TIME RANGE CODE WILL ALSO CHANGE FROM 018 TO 2004.
 SDIS USING THE TIME RANGE CODE WILL NEED TO BE UPDATED.
 FOR FURTHER DETAILS: <http://thomsonderwent.com/chem/polymers/> <<<

=> d all abeq tech abex tot

L88 ANSWER 1 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
 AN 2003-421048 [39] WPIX
 DNC C2003-110745
 TI New hybrid polypeptide, useful for sequestering and/or purifying a
 polypeptide of interest.
 DC B04 D16
 IN THOMAS, T; TILLETT, D
 PA (PROT-N) PROTİGENE PTY LTD
 CYC 101
 PI WO 2003018616 A1 20030306 (200339)* EN 66p C07K001-14
 RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU
 MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
 DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
 KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
 RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA
 ZM ZW

ADT WO 2003018616 A1 WO 2002-AU1159 20020827

PRAI AU 2001-7298 20010827

IC ICM C07K001-14

ICS C07K001-36; **C07K019-00**; C12N009-00; C12N015-63

AB WO2003018616 A UPAB: 20030619

NOVELTY - A hybrid polypeptide comprises a polypeptide of interest linked to a polymerizable polypeptide, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) sequestering and/or purifying a polypeptide of interest;
- (2) a hybrid nucleic acid comprising a nucleic acid encoding the hybrid polypeptide;
- (3) a library comprising several hybrid nucleic acids, polypeptides or vectors;
- (4) a vector comprising the hybrid nucleic acid;
- (5) a cell transformed or transfected with the hybrid nucleic acid or vector; and
- (6) purifying a polypeptide of interest.

USE - The hybrid polypeptide is useful for sequestering and/or purifying a polypeptide of interest (claimed).

Dwg.0/9

FS CPI

FA AB; DCN

MC CPI: B04-B04C; **B04-C01**; B04-E08; B04-F0100E; B04-G01; B04-H01;
 B04-H02B; B04-H04; **B04-H05**; B04-H19; B04-J01; B04-J02;
 B04-J05; B04-J10; B04-L04; B04-L05; B04-L06; B04-L07; B04-N03;
 B04-N04; B04-N06; B04-N08; B11-B; D05-C11; D05-H12A; D05-H12E;
 D05-H13; D05-H14; D05-H17C

TECH UPTX: 20030619

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Polypeptide: The hybrid polypeptide is produced in vivo. It is linked to a support, comprising the polymerizable polypeptide. The support polymerizable polypeptide comprises a polymerizable polypeptide identical to the hybrid polypeptide, or its variant. The polypeptide of interest is linked to the polymerizable polypeptide by fusing the polypeptide of interest directly to the polymerizable polypeptide or by a linker polypeptide. It is prokaryotic or eukaryotic in origin. It is a synthetic polypeptide. It comprises endonuclease, a methylase, an oxidoreductase, a transferase, a hydrolase, a lysase, an isomerase, a ligase, a storage polypeptide, a ferritin, an **ovalbumin**, a transport protein, hemoglobin, serum **albumin** or ceruloplasmin, an antigen, an antigenic determinant for use in the preparation of vaccines or diagnostic agents, a protective protein, a defense protein, thrombin, fibrinogen, binding proteins, antibodies, immunoglobulins, a human growth hormone, somatostatin, prolactin, estrange, progesterone, melanocyte, thyrotropin, calcitonin, gonadotropin, insulin, a hormone identified as being involved in the immune system, interleukin 1, interleukin 2, colony simulating factor, macrophage-activating factor, interferon, a structural element, collagen, elastin, alpha-keratin, glyco-protein, virus-protein and muca-protein. The linker polypeptide comprises a recognition site for a proteolytic agent and a multiple cloning site. It also comprises a spacer polypeptide of sufficient length to allow or enhance cleavage of the polypeptide of interest from the polymerizable polypeptide, or to avoid unfavorable steric interference between the polypeptide of interest and the polymerizable polypeptide. The recognition site comprises an amino acid sequence consisting of:
 (a) Leu-Glu-Val-Leu-Phe-Gln-Gly-Pro;
 (b) Leu-Val-Pro-Arg-Gly-Ser;

- (c) Ile-Glu-Gly-Arg; or
- (d) Asp-Asp-Asp-Asp-Lys.

The chemical capable of proteolytic activity is cyanogen bromide. The polypeptides are linked by antibody interaction, which is achieved by:

- (a) attaching an antibody specific for the polypeptide of interest to the polymerizable polypeptide; or

- (b) using a bi-specific antibody directed to both the polypeptide of interest and the polymerizable polypeptide.

The polymerizable polypeptide is a polypeptide that naturally polymerizes with itself. It is tubulin or actin. It is an FtsZ or Escherichia coli FtsZ protein or its variant. The variant Escherichia coli FtsZ protein comprises replacement of the aspartate residue at position 212 of the protein with a cysteine or asparagine residue. The variant FtsZ protein comprises a mutation selected from replacement of alanine by threonine at position 70, replacement of aspartate by alanine at position 209 or replacement of aspartate by alanine at position 269. The polymerizable polypeptide requires an intermediary polypeptide or other molecule in order to polymerize.

Preferred Method: Sequestering and/or purifying a polypeptide of interest comprises polymerizing the hybrid polypeptide under controlled chemical and/or physical conditions. It is polymerized by a change in temperature and by the addition of an agent that induces polymerization. The polymerization inducing agent is GTP, ATP and/or a cation. The cation comprises magnesium, calcium, nickel, cobalt, zinc or manganese. The polymerized hybrid polypeptide is purified by a first purification step, which may be the only purification step or may be followed by further purification steps. The first purification step purifies the polymerized hybrid polypeptide by physical techniques discriminating on the basis of size and/or weight. The polymerized hybrid polypeptide is also purified by centrifugation, differential sedimentation, filtration, dialysis and/or flow sorting, where the polymerized hybrid polypeptide is isolated. After the first purification step the polymerized hybrid polypeptide is dissociated. The dissociation is achieved by removal of the agent which induces polymerization and/or incubation of the polymerized hybrid polypeptide at a suitable temperature. The dissociated hybrid polypeptide is purified by a second purification step, which comprises purification of the hybrid polypeptide on the basis of size and/or weight. The polymerization, dissociation and purification of the polymerizable hybrid polypeptide are repeated so that substances larger and smaller than the hybrid polypeptide are removed. The polymerizable polypeptide is cleaved from the polypeptide of interest by a proteolytic agent, which does not substantially interfere with the biological or chemical activity of the polypeptide of interest or the polymerizable polypeptide. After the cleavage of the polypeptide of interest from the polymerizable polypeptide, the protease hybrid polypeptide is polymerized. The proteolytic agent comprises 3C-protease from a human rhinovirus type 14 (HRV protease 3C), thrombin, Factor Xa, enterokinase and a chemical capable of proteolytic activity. It is linked to a polymerizable polypeptide to form a protease hybrid polypeptide. The polymerizable polypeptide to which the protease is linked is identical to the polymerizable polypeptide to which the polypeptide of interest is linked, or is a variant of it.

Purifying a polypeptide of interest comprises:

- (a) expressing the hybrid nucleic acid in a cell to produce a hybrid polypeptide comprising the polypeptide of interest and a polymerizable polypeptide;
- (b) polymerizing the hybrid polypeptide;
- (c) purifying the polymerized hybrid polypeptide;
- (d) cleaving the polypeptide of interest from the polymerizable polypeptide; and
- (e) purifying the polypeptide of interest.

L88 ANSWER 2 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
 AN 2002-179329 [23] WPIX
 CR 2001-602931 [68]
 DNC C2002-055553
 TI New **albumin** fusion proteins with extended shelf life, useful for treating leukemia, warts, hepatitis, multiple sclerosis and AIDS, comprises therapeutic protein fused to **albumin**.
 DC B04 D16
 IN BALLANCE, D J; PRIOR, C P; SADEGHI, H; SLEEP, D; TURNER, A J
 PA (DELZ) DELTA BIOTECHNOLOGY LTD; (PRIN-N) PRINCIPIA PHARM CORP; (BALL-I) BALLANCE D J; (PRIO-I) PRIOR C P; (SADE-I) SADEGHI H; (SLEE-I) SLEEP D; (TURN-I) TURNER A J
 CYC 96
 PI WO 2001079271 A1 20011025 (200223)* EN 294p C07K014-00
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
 DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
 LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD
 SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 2001061024 A 20011030 (200225) C07K014-00
 EP 1278767 A1 20030129 (200310) EN C07K014-00
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI TR
 US 2003199043 A1 20031023 (200370) C12P021-02
 JP 2003530839 W 20031021 (200373) 453p C12N015-09
 ADT WO 2001079271 A1 WO 2001-US12009 20010412; AU 2001061024 A AU 2001-61024
 20010412; EP 1278767 A1 EP 2001-934875 20010412, WO 2001-US12009 20010412;
 US 2003199043 A1 Provisional US 2000-229358P 20000412, Provisional US
 2000-199384P 20000425, Provisional US 2000-256931P 20001221, US
 2001-832501 20010412; JP 2003530839 W JP 2001-576866 20010412, WO
 2001-US12009 20010412
 FDT AU 2001061024 A Based on WO 2001079271; EP 1278767 A1 Based on WO
 2001079271; JP 2003530839 W Based on WO 2001079271
 PRAI US 2000-256931P 20001221; US 2000-229358P 20000412; US 2000-199384P
 20000425; US 2001-832501 20010412
 IC ICM C07K014-00; C12N015-09; C12P021-02
 ICS A61K038-00; A61K038-16; **A61K038-21**; A61K038-43; A61K038-46;
 A61K038-48; A61K038-55; A61K039-395; A61K047-48; A61P001-16;
 A61P015-00; A61P017-12; A61P025-28; A61P031-12; A61P031-14;
 A61P031-18; A61P031-20; A61P035-00; A61P035-02; C07H021-04;
 C07K014-52; C07K014-56; C07K014-745; C07K014-75;
 C07K014-76; C07K014-765; C07K014-81; C07K016-00;
 C07K019-00; C12N001-19; C12N001-21; C12N005-06; C12N005-10;
 C12N009-14; C12N009-74; C12N009-99; C12N015-00
 AB WO 200179271 A UPAB: 20031112
 NOVELTY - An **albumin** fusion protein (I) comprising:
 (a) a therapeutic protein (X) and **albumin** (A) containing a fully defined sequence (S1) of 585 amino acids as given in the specification;
 (b) X and a fragment or variants of S1, where the fragment or variants has **albumin** activity; or
 (c) a fragment or variant of X and A, where the fragment or variant has a biological activity of X, is new.
 DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
 (1) an **albumin** fusion protein (II) comprising a peptide inserted into A comprising amino acids 54-61, 76-89, 92-100, 170-176, 247-252, 266-277, 280-288, 362-368, 439-447, 462-475, 478-486 or 560-566 of S1;
 (2) an **albumin** fusion protein (III) comprising a single chain antibody or its portion and A or its fragment or variant;

- (3) a composition comprising any of (I)-(III) and a pharmaceutically active carrier;
- (4) a kit comprising the composition;
- (5) treating a disease or disorder that is modulated by X in a patient comprising administering any of (I)-(III);
- (6) extending the shelf life of X comprising fusing X or its fragment or variant to A or its fragment or variant, sufficient to extend the shelf-life of X compared to the shelf life of X in an unfused state;
- (7) a nucleic acid molecule (IV) comprising a polynucleotide sequence encoding any of (I)-(III);
- (8) a vector comprising (IV); and
- (9) a host cell comprising (IV).

ACTIVITY - Cytostatic; dermatological; virucide; anti-HIV; neuroprotective; hepatotropic; antiinflammatory. Tests are described but no results are given in the source material.

MECHANISM OF ACTION - Gene therapy.

USE - The fusion protein is useful for the treatment of hairy cell leukemia, Kaposi's sarcoma, genital warts, anal warts, chronic hepatitis B, chronic non-A, non-B hepatitis, hepatitis C/D, chronic myelogenous leukemia, renal cell carcinoma, bladder carcinoma, ovarian carcinoma, cervical carcinoma, skin cancer, recurrent respiratory papillomatosis, non-Hodgkin's lymphoma, cutaneous T-cell lymphoma, melanoma, multiple myeloma, acquired immunodeficiency syndrome (AIDS), multiple sclerosis and glioblastoma. The fusion of **albumin** extends the shelf life and the *in vivo* and *in vitro* biological activity of the therapeutic protein (all claimed).

ADVANTAGE - Therapeutic proteins can be stabilized to extend shelf life and/or retain the protein's activity for extended periods of time in solution, *in vivo* or *in vitro* by genetically or chemically fusing the protein to **albumin** or its fragment or variant. In addition the use of **albumin** fusion proteins reduces the need to formulate protein solutions with large excesses of carrier proteins to prevent loss of therapeutic protein due to factors such as binding to the container. The extension of shelf life was tested by measuring biological activity (Nb2 cell proliferation) of human **albumin**-human growth hormone (HA-hGH) fusion protein remaining after incubation in cell culture media for up to 3 weeks at 37 deg. C. At week 3 there was still approx. 95% cell proliferation compared to no activity of unfused hGH (no observed activity by week 2).

Dwg.0/18

FS	CPI
FA	AB; DCN
MC	CPI: B04-C01G ; B04-E02H; B04-E08; B04-F0100E; B04-G01; B04-H05A ; B04-H19; B04-L05A; B04-N02A ; B04-N08; B14-A02A; B14-A02B1; B14-G01B; B14-H01; B14-N12; B14-N17; B14-S01; B14-S03A; D05-C12; D05-H12C; D05-H12E; D05-H14; D05-H17C

TECH UPTX: 20020411
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: The fusion proteins can be prepared by standard recombinant techniques.

Preferred Fusion Protein: **Albumin** activity is the ability to prolong the shelf life of X compared to the shelf life of X in an unfused state. Preferably the fragment or variant of (I) comprises amino acids 1-387 of S1. X is chosen from serum cholinesterase, alpha-1 antitrypsin, aprotinin, coagulated complex, von Willebrand factor, fibrinogen, factor VII, factor VIIA activated factor, factor VIII, factor IX, factor X, factor XIII, c1 inactivator, antithrombin III, thrombin, prothrombin, apo-lipoprotein, c-reactive protein, protein C, immunoglobulin and preferably interferon (IFN)-alpha. X or its fragment or variant is fused to the N or C-terminus of A. (I)-(III) comprises a first and second X, where the first X is different from the second X. X is separated from A by a linker. The fusion protein has the formula R1-L-R2, R2-L-R1 or R1-L-R2-L-R1, where:

R1 = X

L = peptide linker; and

R2 = A or its fragment or variant.

The in vitro or in vivo activity of X fused to A is greater than the in vitro or in vivo biological activity of X in an unfused state. The protein is expressed in a glycosylation and protease deficient yeast.

Alternatively it is expressed by a mammalian cell in culture. The fusion protein further comprises a secretion leader sequence.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: The fusion proteins can be produced by standard chemical synthetic techniques.

ABEX UPTX: 20020411

ADMINISTRATION - 1 microgram/kg/day to 10 mg/kg/day, preferably 0.01-1 mg/kg/day of **albumin** fusion proteins are administered by standard routes.

EXAMPLE - A human **albumin**-human growth hormone (HA-hGH) fusion protein was prepared. The hGH cDNA was obtained from a human pituitary gland cDNA library by polymerase chain reaction (PCR) amplification. The PCR product was purified and then digested with EcoR1 and HindIII. After further purification of the EcoR1-HindIII fragment by gel electrophoresis, the product was cloned into pUC19 digested with EcoR1 and HindIII to give pHGH1. The polylinker sequence of the phagemid pBluescribe (+) (Stratagene) was replaced by inserting an oligonucleotide linker formed by annealing 2 75-mer oligonucleotides between the EcoR1 and HindIII sites to form pBST(+). The new polylinker included a unique NotI site. The NotI HA expression cassette of pAYE309 comprising the PRBI promoter, DNA encoding the HA/MFalpha-1 hybrid leader sequence, DNA encoding HA and the ADH1 terminator, was transferred to pBST(+) to form pHAl. The HA sequence was removed from this plasmid by digestion with HindIII followed by religation to form pHG2. Cloning of the hGH cDNA provided the hGH coding region lacking the pro-hGH sequence and the first 8 base pairs (bp) of the mature hGH sequence. In order to construct an expression plasmid for secretion of hGH from yeast, a yeast promoter, signal peptide and the first bp of the hGH sequence were attached to the 5' end of the cloned hGH sequence. The HindIII-SfaNI fragment from pHAl was attached to the 5' end of the EcoR1/HindIII fragment from pHGH1 via 2 synthetic oligonucleotides to generate a double stranded fragment of DNA with sticky ends that can anneal with SfaNI and EcoR1 sticky ends. The HindIII fragment formed was cloned into HindIII digested pHG2 to make pHGH2 such that the hGH cDNA was positioned downstream of the PRBI promoter and HA/MFalpha-1 fusion leader sequence. The NotI expression cassette contained in pHGH2 was cloned into the NotI-digested pSAC35 to make pHGH12. This plasmid comprised the entire 2 micro m plasmid to provide replication functions and the LEU2 gene for selection of transformants. pHGH12 was introduced into *S. cerevisiae* D88 by transformation and individual transformants were grown for 3 days at 30 degrees C in 10 mL YEPD (1% w/v yeast extract, 2% w/v peptone, 2% w/v dextrose). After centrifugation of the cells, the supernatants were examined by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and were found to contain protein which was of the expected size and recognized by anti-hGHG antiserum on Western blots.

L88 ANSWER 3 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2001-616754 [71] WPIX

CR 2001-602931 [68]; 2001-611723 [70]; 2001-616755 [71]; 2001-616756 [71];
2002-010886 [01]; 2003-810996 [76]; 2004-033644 [03]

DNC C2001-184720

TI **Albumin** fusion proteins comprising a therapeutic protein and **albumin**, useful in the treating immune system disorders (e.g. transplant rejection), blood related disorders (e.g. myocardial infarction) and hyperproliferative disorders.

DC B04 D16

IN HASELTINE, W A; ROSEN, C A

PA (HUMA-N) HUMAN GENOME SCI INC

CYC 96

PI WO 2001079443 A2 20011025 (200171)* EN 365p C12N000-00
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
 DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
 LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD
 SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 2001059063 A 20011030 (200219) C12N000-00
 EP 1274719 A2 20030115 (200313) EN C07K001-00
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI TR
 JP 2003530846 W 20031021 (200373) 469p C12N015-09
 ADT WO 2001079443 A2 WO 2001-US11924 20010412; AU 2001059063 A AU 2001-59063
 20010412; EP 1274719 A2 EP 2001-932546 20010412, WO 2001-US11924 20010412;
 JP 2003530846 W JP 2001-577427 20010412, WO 2001-US11924 20010412
 FDT AU 2001059063 A Based on WO 2001079443; EP 1274719 A2 Based on WO
 2001079443; JP 2003530846 W Based on WO 2001079443
 PRAI US 2000-256931P 20001221; US 2000-229358P 20000412; US 2000-199384P
 20000425
 IC ICM C07K001-00; C12N000-00; C12N015-09
 ICS A01N037-18; A61K038-00; **A61K038-21**; A61K038-28;
 A61K039-395; A61K047-48; A61K048-00; A61P001-16; A61P013-00;
 A61P025-00; A61P031-14; A61P031-18; A61P031-20; A61P035-00;
 A61P035-02; C07K014-47; **C07K014-76**; **C07K019-00**;
 C12N001-19; C12N005-10
 AB WO 200179443 A UPAB: 20040112
 NOVELTY - **Albumin** fusion proteins (P1) comprising a therapeutic protein (T1) (or its fragment or variant having the activity of T1) and **albumin** comprising the 585 amino acid sequence (I) defined in the specification (or its fragment or variant having **albumin** activity), are new.
 DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
 (1) a kit comprising a composition containing P1;
 (2) a method of treating a disease or disorder, preferably modulated by T1, in a patient, comprising administering P1;
 (3) a method of extending the shelf-life of T1, comprising fusing T1 or its fragment or variant, to **albumin** or its fragment or variant, where the shelf-life of T1 or its fragment or variant as part of a fused protein is extended when compared to T1 or its fragment or variant in an unfused state;
 (4) a nucleic acid (N1) comprising a nucleotide sequence encoding P1;
 (5) a vector comprising N1; and
 (6) a host cell comprising N1.
 ACTIVITY - Cytostatic; antiinflammatory; antileukemic; antiarthritic; antirheumatic; immunosuppressive; cardiant; nootropic; neuroprotective; antimicrobial; vulnerary.
 To test whether sympathetic neuronal cell viability is supported by an **albumin** fusion protein, the chicken embryo neuronal survival assay (Senaldi, et al., Proc. Natl. Acad. Sci., U.S.A., 96:11458-63 (1998)). Briefly, motor and sympathetic neurons were isolated from chicken embryos, resuspended in L15 medium (with 10% foetal calf serum (FCS), glucose, sodium selenite, progesterone, **conalbumin**, putrescine and insulin) and Dulbecco's modified Eagles medium (with 10% FCS, glutamine, penicillin, and 25 mM Hepes buffer (pH 7.2)), respectively and incubated at 37 degrees Centigrade in 5% carbon-dioxide in the presence of different concentrations of the purified fusion protein, as well as negative control lacking any cytokine. After 3 days, neuronal survival was determined by evaluation of cellular morphology, and through the use of the colorimetric assay of Mosmann (Mosmann, T., J. Immunol., Methods, 65:55-63 (1983)). Enhanced neuronal cell viability as compared to the controls lacking cytokine is indicative of the ability of the **albumin** fusion protein to enhance the survival of neuronal cells.

MECHANISM OF ACTION - Gene therapy.

USE - The **albumin** fusion proteins are also useful in the treatment, prevention, diagnosis, and/or detection of diseases, disorders such as immune system disorders (e.g. transplant rejection), blood related disorders (e.g. myocardial infarction), hyperproliferative disorders (e.g. childhood acute myeloid leukemia), renal disorders (e.g. glomerulonephritis), cardiovascular disorders (e.g. arrhythmias), respiratory disorders (e.g. non-allergic rhinitis), neurological diseases (e.g. Alzheimer's disease), endocrine disorders (e.g. pheochromocytoma), reproductive system disorders (e.g. syphilis), infectious diseases (e.g. measles), gastrointestinal disorders (e.g. irritable bowel syndrome) and wound healing.

Dwg.0/15

FS

CPI

FA

AB; DCM

MC

CPI: **B04-C01**; B04-E02F; B04-E08; B04-F0100E; B04-F0200E;
B04-F0900E; B04-F1100E; **B04-N02A0E**; B14-A01; B14-A02;
B14-D01; B14-E10; B14-F01; B14-F02; B14-G01; B14-G02; B14-G03;
B14-H01; B14-J01; B14-K01; B14-N10; B14-N17B; B14-S03;
D05-H12B2; D05-H12E; D05-H14A2; D05-H14B2

TECH

UPTX: 20011203

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Fusion Protein: The **albumin** activity is the ability to prolong the shelf-life of T1 compared to the shelf-life of T1 in an unfused state. The **albumin** fragment or variant comprises amino acids 1-387 of (I).

T1 or its fragment or variant is fused to the C-terminal of the **albumin** or the C-terminus of the fragment or variant of **albumin**. Alternatively, T1 or its fragment or variant is fused to the N-terminal of the **albumin** or the N-terminus of the fragment or variant of **albumin**. Alternatively, T1 or its fragment or variant is fused to the N-terminus and C-terminus of the **albumin**, or the N-terminus and C-terminus of the fragment or variant of **albumin**.

P1 comprises a first T1 or its fragment or variant, and a second T1 or its fragment or variant, where the first T1 is different from the second T1. T1 or its fragment or variant is separated from the **albumin** or the fragment or variant of **albumin** by a linker. Preferably, P1 is of the formula (S1), (S2) or (S3).

R1-L-R2 (S1);
R2-L-R1 (S2); or
R1-L-R2-L-R1 (S3).

Where

R1 = is T1 or its fragment or variant;

L = is a peptide linker; and

R2 = is **albumin** comprising the sequence of (I), or its fragment or variant.

The shelf-life of the **albumin** fusion protein is greater than the shelf-life of T1 or its fragment or variant in an unfused state.

The in vitro or in vivo biological activity of T1 or its fragment or variant, fused to **albumin** or its fragment or variant, is greater than the in vitro or in vivo, respectively, biological activity of T1 or its fragment or variant, in an unfused state.

Alternatively, P1 comprises T1 or its fragment or variant, inserted into an **albumin** comprising the sequence of (I) or its fragment or variant. Preferably, the **albumin** comprises residues 54-61, 76-89, 92-100, 170-176, 247-252, 266-277, 280-288, 362-368, 439-447, 462-475, 478-486, or 560-566 of (I). The portion of **albumin** is sufficient to prolong the shelf-life of T1, or its fragment or variant, as compared to the shelf-life of T1, or its fragment or variant in an unfused state.

The portion of **albumin** is sufficient to prolong the in vitro and in vivo biological activity of T1 or its fragment or variant, as compared to the in vitro and in vivo biological activity of T1 or its fragment or

variant, in an unfused state.

P1 is non-glycosylated and is expressed in yeast which is glycosylation deficient. The yeast may also be protease deficient. Alternatively, P1 is expressed by a mammalian cell in culture. P1 further comprises a secretion leader sequence.

ABEX UPTX: 20011203

ADMINISTRATION - The **albumin** fusion proteins can be administered orally, rectally, parenterally, intracisternally, intravaginally, intraperitoneally, topically, buccally, or as an oral or nasal spray. The dosage is 1 microgram/kg/day to 10 mg/kg/day, preferably 0.01 to 1, mg/kg/day. If given continuously, the **albumin** fusion protein is typically administered at a dose rate of 1-50 micrograms/kg/hour, either by 1-4 injections per day or by continuous subcutaneous infusions.

L88 ANSWER 4 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2001-611723 [70] WPIX

CR 2001-602931 [68]; 2001-616754 [71]; 2001-616755 [71]; 2001-616756 [71];
2002-010886 [01]; 2003-810996 [76]; 2004-033644 [03]

DNC C2001-182838

TI New **albumin** fusion proteins, useful for treating diseases and disorders such as cancer, comprise therapeutic protein fused to **albumin**.

DC B04 D16

IN HASELTINE, W A; ROSEN, C A

PA (HUMA-N) HUMAN GENOME SCI INC

CYC 96

PI WO 2001079442 A2 20011025 (200170)* EN 362p C12N000-00

 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW

 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
 DM DZ EE ES FFI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
 LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD
 SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

 AU 2001064563 A 20011030 (200219) C12N000-00

 EP 1276849 A2 20030122 (200315) EN C12N001-18

 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI TR

 JP 2003531590 W 20031028 (200373) 540p C12N015-09

ADT WO 2001079442 A2 WO 2001-US11850 20010412; AU 2001064563 A AU 2001-64563
20010412; EP 1276849 A2 EP 2001-938994 20010412, WO 2001-US11850 20010412;
JP 2003531590 W JP 2001-577426 20010412, WO 2001-US11850 20010412

FDT AU 2001064563 A Based on WO 2001079442; EP 1276849 A2 Based on WO
2001079442; JP 2003531590 W Based on WO 2001079442

PRAI US 2000-256931P 20001221; US 2000-229358P 20000412; US 2000-199384P
20000425

IC ICM C12N000-00; C12N001-18; C12N015-09

ICS A61K038-00; **A61K038-21**; A61K039-395; A61K048-00;
A61P001-04; A61P001-16; A61P001-18; A61P003-10; A61P005-14;
A61P005-40; A61P007-04; A61P007-06; A61P009-00; A61P009-06;
A61P009-10; A61P009-12; A61P011-00; A61P011-06; A61P013-00;
A61P013-02; A61P013-08; A61P013-12; A61P015-00; A61P015-10;
A61P015-18; A61P017-00; A61P017-02; A61P019-00; A61P019-02;
A61P019-08; **A61P021-00**; A61P021-04; A61P025-00; A61P025-08;
A61P025-16; A61P025-28; A61P027-02; A61P029-00; A61P031-00;
A61P031-12; A61P031-16; A61P031-18; A61P031-22; A61P033-02;
A61P033-06; A61P033-12; A61P035-00; A61P035-02; A61P037-00;
A61P037-08; A61P039-02; A61P041-00; A61P043-00; C07K014-47;
C07K014-76; C07K019-00; C12N001-19; C12N005-10

AB WO 200179442 A UPAB: 20040112

NOVELTY - An **albumin** fusion protein (I) comprising a therapeutic protein: X and (a fragment or variant of) **albumin** comprising a fully defined sequence (S18) of 585 amino acids as given in the specification, (where the fragment or variant has **albumin** or

therapeutic protein: X activity) is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) a kit comprising a composition containing (I);
- (2) treating a disease or disorder (that is modulated by therapeutic protein: X or its fragment or variant) comprising administering (I);
- (3) extending the shelf life of therapeutic protein: X comprising fusing therapeutic protein: X or its fragment or variant to **albumin** or its fragment or variant, sufficient to extend the shelf life of therapeutic protein: X compared to the shelf life of therapeutic protein: X in an unfused state;
- (4) a nucleic acid molecule (II) comprising a polynucleotide sequence encoding (I);
- (5) a vector comprising (II); and
- (6) a host cell comprising (II).

ACTIVITY - Cytostatic; anorectic; immunosuppressive; antidiabetic; antirheumatic; antiarthritic; psoriatic. No supporting data is given.

MECHANISM OF ACTION - None given.

USE - **Albumin** fusion proteins are stabilized therapeutic proteins e.g. antibodies to C5, C242 and CD80 useful for treating various diseases and disorders such as non-Hodgkin's lymphoma, cancer, obesity, transplant rejection, type I diabetes mellitus, rheumatoid arthritis and psoriasis.

ADVANTAGE - Fusing **albumin** to therapeutic proteins stabilizes the therapeutic protein, extends the shelf life and retains the in vitro or in vivo biological activity. It also reduces the need to formulate protein solutions with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. The fusion proteins are easily dispensed with a simple formulation requiring minimal post storage manipulation.

The fusion of therapeutic proteins to **albumin** confers stability in aqueous or other solution. A solution of 200 microgram/ml of human **albumin** (HA)-human growth hormone (hGH) was prepared in tissue culture media containing 5% horse serum and the solution incubated at 37 degrees C starting at time zero. A sample was removed and tested for its biological activity in the Nb2 cell assay at 2 ng/ml final concentration. The biological activity of HA-gHG remained essentially intact after 5 weeks of incubation at 37 degrees C. The recombinant hGH used as control lost its biological activity in the first week of the experiment.

Dwg.0/20

FS

CPI

FA

AB; DCN

MC

CPI: B04-B04D4; B04-E02F; B04-E03A; B04-E08; B04-F0100E; B04-G01;
B04-N02B0E; B04-P0100E; B11-C07A; B12-K04A; B14-C09B;
 B14-E12; B14-G02C; B14-H01; B14-N17C; B14-S04; D05-H11; D05-H12A;
 D05-H12C; D05-H12E; D05-H14; D05-H16; D05-H17C; D05-H17C1

TECH

UPTX: 20011129

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Protein: The **albumin** activity is the ability to prolong the shelf life of the therapeutic protein: X compared to the shelf life of therapeutic protein: X in the unfused state. (I) has a greater shelf life than the therapeutic protein: X in the unfused state. The in vitro or in vivo biological activity of (I) is greater than the in vitro or in vivo activity of therapeutic protein: X or its fragment or variant in an unfused state. (I) comprises 2 therapeutic protein: X or their fragments or variants, which are different from each other. Therapeutic protein: X or its fragment or variant is separated from the **albumin** or its fragment or variant by a linker. (I) comprises a therapeutic protein: X or its fragment or variant I-inserted into an **albumin** comprising amino acids 54-61, 76-89, 92-100, 170-176, 247-252, 266-277, 280-288, 362-368, 439-447, 462-475, 478-486 or 560-566 of S18. (I) further comprises a secretion leader sequence. (I) has the formula: R1-L-R2; R2-L-R1; or R1-L-R2-L-R1, where:

R1 = therapeutic protein: X or its fragment or variant;

L = peptide linker; and

R2 = **albumin** comprising S18.

(I) is non-glycosylated and expressed in a glycosylation and protease deficient yeast cell. Alternatively (I) is expressed in a mammalian cell in culture.

Preferred Method: The disease or disorder comprises indication: Y.

Preparation: (I) are prepared by standard recombinant techniques.

ABEX UPTX: 20011129

WIDER DISCLOSURE - Also disclosed as new are:

- (1) transgenic organisms modified to contain (II) to express (I);
- (2) antibodies that bind to a therapeutic protein;
- (3) generating antibodies that bind to a therapeutic protein;
- (4) polynucleotides encoding the antibody;
- (5) diagnosing a disorder comprising assaying the expression of the therapeutic protein in cells or body fluid of an individual using antibodies specific to the therapeutic protein and comparing the level of gene expression with a standard gene expression level, where an increase or decrease in the assayed gene expression level is indicative of a particular disorder; and
- (6) a diagnostic kit for use in screening serum containing antigens of a therapeutic protein comprising an antibody immunoreactive with the antigen.

ADMINISTRATION - 0.1-100 mg/kg of body weight, preferably 1-10 mg/kg of body weight of antibodies are administered by standard routes.

EXAMPLE - Preparation of human **albumin** fusion proteins was as follows. The cDNA for interferon (IFN) alpha was isolated from cDNA libraries by reverse transcription-polymerase chain reaction (PCR) and by PCR using a series of overlapping synthetic oligonucleotides primers using standard methods. The cDNA was tailored at the 5' and 3' ends to generate restriction sites so that oligonucleotide linkers could be used to clone the cDNA into a vector containing the cDNA for human **albumin** (HA). This could be at the N or C terminus of the HA sequence with (out) use of a spacer sequence. The IFN alpha cDNA was cloned into a vector such as pPPC0005 from which the complete expression cassette was excised and inserted into the plasmid pSAC35 to allow the expression of the **albumin** fusion protein in yeast. The **albumin** fusion protein was collected and purified from the media and tested for its biological activity.

L88 ANSWER 5 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
 AN 2001-602931 [68] WPIX
 CR 2001-611723 [70]; 2001-616754 [71]; 2001-616755 [71]; 2001-616756 [71];
 2002-010886 [01]; 2002-179329 [23]; 2003-810996 [76]; 2004-033644 [03]
 DNC C2001-178694
 TI **Albumin** fusion proteins comprising a therapeutic protein and **albumin**, useful in the treating metastatic renal cell carcinoma, metastatic melanoma, malignant melanoma, renal cell carcinoma, HIV (human immunodeficiency virus) or infection.
 DC B04 D16
 IN PRIOR, C P; ROSEN, C A; SADEGHI, H; TURNER, A J
 PA (HUMA-N) HUMAN GENOME SCI INC; (PRIN-N) PRINCIPIA PHARM CORP; (PRIO-I)
 PRIOR C P; (ROSE-I) ROSEN C A; (SADE-I) SADEGHI H; (TURN-I) TURNER A J
 CYC 96
 PI WO 2001079258 A1 20011025 (200168)* EN 325p C07K001-00
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
 DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
 LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD
 SE SG SI SK SL TJ TM TT TZ UA UG US UZ VN YU ZW

AU 2001059066 A 20011030 (200219) C07K001-00
 EP 1274720 A1 20030115 (200313) EN C07K001-00
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI TR

US 2003171267 A1 20030911 (200367) A61K038-38 <--
 JP 2003530838 W 20031021 (200373) 430p C12N015-09

ADT WO 2001079258 A1 WO 2001-US12008 20010412; AU 2001059066 A AU 2001-59066
 20010412; EP 1274720 A1 EP 2001-932549 20010412, WO 2001-US12008 20010412;
 US 2003171267 A1 Provisional US 2000-229358P 20000412, Provisional US
 2000-199384P 20000425, Provisional US 2000-256931P 20001221, US
 2001-833117 20010412; JP 2003530838 W JP 2001-576855 20010412, WO
 2001-US12008 20010412

FDT AU 2001059066 A Based on WO 2001079258; EP 1274720 A1 Based on WO
 2001079258; JP 2003530838 W Based on WO 2001079258

PRAI US 2000-256931P 20001221; US 2000-229358P 20000412; US 2000-199384P
 20000425; US 2001-833117 20010412

IC ICM **A61K038-38**; C07K001-00; C12N015-09
 ICS A01N037-18; A61K035-12; A61K035-76; A61K038-00; **A61K038-21**;
 A61K038-22; A61K038-23; A61K038-27; A61K047-48; A61K048-00;
 A61P001-04; A61P003-10; A61P003-14; A61P005-10; A61P009-10;
 A61P015-08; A61P017-00; A61P017-02; A61P017-06; A61P017-14;
 A61P019-00; A61P019-02; A61P019-08; A61P019-10; A61P021-00;
 A61P025-00; A61P025-02; A61P025-28; A61P029-00; A61P031-14;
A61P031-18; A61P031-20; A61P035-00; A61P035-02; A61P035-04;
 A61P037-00; A61P037-06; C07K014-55; C07K014-565; C07K014-585;
 C07K014-60; C07K014-62; C07K014-635; C07K014-76; C07K014-765;
 C07K019-00; C12N001-19; C12N005-10

AB WO 200179258 A UPAB: 20040112
 NOVELTY - **Albumin** fusion proteins (P1) comprising a therapeutic protein (T1) (or its fragment or variant having the activity of T1) and **albumin** comprising the 585 amino acid sequence (I) defined in the specification (or its fragment or variant having **albumin** activity), are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) a kit comprising a composition containing P1;
- (2) a method of treating a disease or disorder, preferably modulated by T1, in a patient, comprising administering P1;
- (3) a method of extending the shelf-life of T1, comprising fusing T1 or its fragment or variant, to **albumin** or its fragment or variant, where the shelf-life of T1 or its fragment or variant as part of a fused protein is extended when compared to T1 or its fragment or variant in an unfused state;
- (4) a nucleic acid (N1) comprising a nucleotide sequence encoding P1;
- (5) a vector comprising N1; and
- (6) a host cell comprising N1.

ACTIVITY - Cytostatic; antiviral; antiinflammatory; antileukemic; antiarthritic; antirheumatic; immunosuppressive; antidiabetic; cardiant; nootropic; neuroprotective; antimicrobial; vulnerary.

To test whether sympathetic neuronal cell viability is supported by an **albumin** fusion protein, the chicken embryo neuronal survival assay (Senaldi, et al., Proc. Natl. Acad. Sci., U.S.A., 96:11458-63 (1998)). Briefly, motor and sympathetic neurons were isolated from chicken embryos, resuspended in L15 medium (with 10% fetal calf serum (FCS), glucose, sodium selenite, progesterone, **conalbumin**, putrescine and insulin) and Dulbecco's modified Eagles medium (with 10% FCS, glutamine, penicillin, and 25 mM Hepes buffer (pH 7.2)), respectively and incubated at 37 degrees Centigrade in 5% carbon-dioxide in the presence of different concentrations of the purified fusion protein, as well as negative control lacking any cytokine. After 3 days, neuronal survival was determined by evaluation of cellular morphology, and through the use of the colorimetric assay of Mosmann (Mosmann, T., J. Immunol., Methods, 65:55-63 (1983)). Enhanced neuronal cell viability as compared to the

controls lacking cytokine is indicative of the ability of the **albumin** fusion protein to enhance the survival of neuronal cells.

MECHANISM OF ACTION - Gene therapy.

USE - When the therapeutic protein, or its fragment or variant is IL-2, P1 is used to treat metastatic renal cell carcinoma, metastatic melanoma, malignant melanoma, renal cell carcinoma, HIV (human immunodeficiency virus) infection, inflammatory bowel disorder, Kaposi's sarcoma, leukemia, multiple sclerosis, rheumatoid arthritis, transplant rejection, type 1 diabetes mellitus, lung cancer, acute myeloid leukemia, hepatitis C, non-hodgkin's lymphoma or ovarian cancer (claimed).

The **albumin** fusion proteins are also useful in the treatment, prevention, diagnosis, and/or detection of diseases, disorders such as immune system disorders (e.g. transplant rejection), blood related disorders (e.g. myocardial infarction), hyperproliferative disorders (e.g. childhood acute myeloid leukemia), renal disorders (e.g. glomerulonephritis), cardiovascular disorders (e.g. arrhythmias), respiratory disorders (e.g. non-allergic rhinitis), neurological diseases (e.g. Alzheimer's disease), endocrine disorders (e.g. pheochromocytoma), reproductive system disorders (e.g. syphilis), infectious diseases (e.g. measles), gastrointestinal disorders (e.g. irritable bowel syndrome) and wound healing.

Dwg.0/14

FS

CPI

FA

AB; DCN

MC

CPI: **B04-C01**; B04-E02F; B04-E08; B04-F0100E; B04-F1100E;
B04-H05; B04-H06; B04-J04; **B04-N0200E**;
B04-N02A0E; B14-A02B1; B14-C09B; B14-D01; B14-E10C; B14-F01;
B14-F02; B14-G02; B14-H01; B14-J01; B14-K01; B14-N10; B14-N12;
B14-N14; B14-N17B; B14-S01; B14-S03; B14-S04; **D05-H12B2**;
D05-H12E; D05-H14

TECH

UPTX: 20011121

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Fusion Protein: The **albumin** activity is the ability to prolong the shelf-life of T1 compared to the shelf-life of T1 in an unfused state. The **albumin** fragment or variant comprises amino acids 1-387 of (I). T1 comprises interleukin 2 (IL-2). The T1 fragment or variant has T cell proliferative activity or T cell activation activity. T1 or its fragment or variant, comprises a protein selected from calcitonin, growth hormone releasing factor, IL-2 fusion protein, insulin-like growth factor-1, **interferon beta** or parathyroid hormone. T1 or its fragment or variant is fused to the C-terminal of the **albumin** or the C-terminus of the fragment or variant of **albumin**. Alternatively, T1 or its fragment or variant is fused to the N-terminal of the **albumin** or the N-terminus of the fragment or variant of **albumin**. Alternatively, T1 or its fragment or variant is fused to the N-terminus and C-terminus of the **albumin**, or the N-terminus and C-terminus of the fragment or variant of **albumin**.

P1 comprises a first T1 or its fragment or variant, and a second T1 or its fragment or variant, where the first T1 is different from the second T1. T1 or its fragment or variant is separated from the **albumin** or the fragment or variant of **albumin** by a linker. Preferably, P1 is of the formula (S1), (S2) or (S3).

R1-L-R2 (S1);

R2-L-R1 (S2); or

R1-L-R2-L-R1 (S3).

where

R1 = is T1 or its fragment or variant;

L = is a peptide linker; and

R2 = is **albumin** comprising the sequence of (I), or its fragment or variant.

The shelf-life of the **albumin** fusion protein is greater than the shelf-life of T1 or its fragment or variant in an unfused state. The in vitro or in vivo biological activity of T1 or its fragment or

variant, fused to **albumin** or its fragment or variant, is greater than the in vitro or in vivo, respectively, biological activity of T1 or its fragment or variant, in an unfused state.

Alternatively, P1 comprises T1 or its fragment or variant, inserted into an **albumin** comprising the sequence of (I) or its fragment or variant. Preferably, the **albumin** comprises residues 54-61, 76-89, 92-100, 170-176, 247-252, 266-277, 280-288, 362-368, 439-447, 462-475, 478-486, or 560-566 of (I). The portion of **albumin** is sufficient to prolong the shelf-life and in vitro and in vivo biological activity of T1 or its fragment or variant, as compared to the shelf-life and in vitro and in vivo biological activity of T1 or its fragment or variant, in an unfused state.

P1 is non-glycosylated and expressed in yeast which is glycosylation deficient. The yeast may also be protease deficient. Alternatively, P1 is expressed by a mammalian cell in culture. P1 further comprises a secretion leader sequence.

ABEX UPTX: 20011121

ADMINISTRATION - The **albumin** fusion proteins can be administered orally, rectally, parenterally, intracisternally, intravaginally, intraperitoneally, topically, buccally, or as an oral or nasal spray. The dosage is 1 microgram/kg/day to 10 mg/kg/day, preferably 0.01 to 1, mg/kg/day. If given continuously, the **albumin** fusion protein is typically administered at a dose rate of 1-50 micrograms/kg/hour, either by 1-4 injections per day or by continuous subcutaneous infusions.

EXAMPLE - The cDNA for the growth factor of interest such as interferon growth factor 1 (IGF-1) can be isolated using a variety of means including but not exclusively, from cDNA libraries, by reverse transcriptase-polymerase chain reaction (PCR) and by PCR using a series of overlapping synthetic oligonucleotide primers, all using standard methods (see GenBank Acc. Number NP-000609). The cDNA can be tailored at the 5' and 3' ends to generate restriction sites, such that the oligonucleotide linkers can be used, for cloning of the cDNA into a vector containing the cDNA for human serum **albumin** (HA). This can be at the N or C-terminus with or without the use of a spacer sequence. The growth factor cDNA was cloned into a vector such as pPPC0005, pScCHSA, pScNHSA or pC4:HSA from which the complete expression cassette is then excised and inserted into the plasmid pSAC35 to allow the expression of the **albumin** fusion protein in yeast. The **albumin** fusion protein secreted from the yeast can then be collected and purified from the media and tested for its biological activity. For expression in mammalian cell lines a similar procedure is adopted except that the expression cassette used employs a mammalian promoter, leader sequence and terminator. This expression cassette is then excised and inserted into a plasmid suitable for the transfection of mammalian cell lines.

L88 ANSWER 6 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 1996-300388 [30] WPIX

DNC C1996-095415

TI New chimeric proteins for treatment of septic shock, psoriasis, cancers etc. - comprise cytokine bonded to polypeptide which is enzymatically inactive in humans, increases half-life and prevents cytokine(s) from crossing blood brain barrier.

DC B04

IN STEELE, A; STROM, T B; ZHENG, X; ZHENG, X X
PA (BETH-N) BETH ISRAEL HOSPITAL ASSOC

CYC 20

PI WO 9618412 A1 19960620 (199630)* EN 58p A61K038-19

RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

W: CA JP

EP 793504 A1 19970910 (199741) EN A61K038-19

R: CH DE FR GB IT LI SE

JP 11501506 W 19990209 (199916) 49p C12N015-09

US 6403077 B1 20020611 (200244) A61K038-20
 US 6410008 B1 20020625 (200246) C07K014-54
 US 2002173628 A1 20021121 (200279) A61K038-52
 US 2003026778 A1 20030206 (200318) A61K038-20

ADT WO 9618412 A1 WO 1995-US16046 19951212; EP 793504 A1 EP 1995-943058
 19951212, WO 1995-US16046 19951212; JP 11501506 W WO 1995-US16046
 19951212, JP 1996-519191 19951212; US 6403077 B1 CIP of US 1994-355502
 19941212, Cont of US 1995-431535 19950428, US 1997-968905 19971106; US
 6410008 B1 US 1994-355502 19941212; US 2002173628 A1 Cont of US
 1994-355502 19941212, US 2002-145481 20020514; US 2003026778 A1 CIP of US
 1994-355502 19941212, Cont of US 1997-968905 19971106, US 2002-145517
 20020514

FDT EP 793504 A1 Based on WO 9618412; JP 11501506 W Based on WO 9618412; US
 2002173628 A1 Cont of US 6410008; US 2003026778 A1 Cont of US 6403077, CIP
 of US 6410008

PRAI US 1995-431535 19950428; US 1994-355502 19941212; US 1997-968905
 19971106; US 2002-145481 20020514; US 2002-145517 20020514

REP 2.Jnl.Ref; US 5231012

IC ICM A61K038-19; A61K038-20; A61K038-52; C07K014-54; C12N015-09
 ICS A61K038-00; **A61K038-21; A61K038-38;** A61K039-395;
C07K014-52; C07K014-525; C07K014-53; C07K014-535;
 C07K014-545; C07K014-55; **C07K014-555; C07K014-76;**
C07K014-765; C07K016-18; C07K016-46; **C07K019-00;**
 C12N009-10; C12N015-02; C12N015-24; C12P021-02

AB WO 9618412 A UPAB: 19960731
 Chimeric protein comprises a cytokine bonded to a polypeptide which is
 enzymatically inactive in humans and which increases the circulating
 half-life of the cytokine in vivo by a factor of 1.
 Also claimed is the use of interleukin-10 (IL-10)/Fc in the preparation
 of a medicament for inhibiting granuloma formation in a patient.

USE - The chimeric proteins can be used to treat conditions for which
 the corresp. cytokines are used, e.g. septic shock, granulomatous
 disorders (e.g. schistosomiasis), multiple sclerosis, psoriasis,
 rheumatoid arthritis, cancers and virus infections. Chimeric proteins
 including a lytic Fc region can also be used to deplete patients of
 suppressor lymphocytes and to treat chronic infections such as those
 associated with suppression of the immune system.

ADVANTAGE - The enzymatically inactive polypeptides extend the
 circulating half-life of the cytokines in vivo by a factor of 10
 (claimed). In addition, they can prevent the cytokines from crossing the
 blood brain barrier and causing adverse side effects.

Dwg.0/15

FS CPI
 FA AB
 MC CPI: B04-B04; B04-G01; B04-H02; B04-H04A; B04-H04C; B04-H08;
B04-N02; B14-A01; B14-C09B; B14-N17C; B14-S01; B14-S06

=> => d his

(FILE 'HOME' ENTERED AT 15:22:31 ON 02 FEB 2004)
 SET COST OFF

FILE 'HCAPLUS' ENTERED AT 15:22:50 ON 02 FEB 2004
 E ALBUMIN/CT

L1	753	S	E3
L2	132	S	E11
			E E47+ALL
L3	80101	S	E2+NT
			E E33+ALL
L4	566	S	E3,E2
L5	25218	S	E2+NT
L6	157881	S	?ALBUMIN?

L7 181833 S L1-L6
L8 2969 S BDNF OR BD NF
L9 2881 S BRAIN DERIVED NEUROTROPHIC FACTOR
L10 2883 S (BD OR BRAIN DERIVED) () (NF OR NEUROTROPHIC FACTOR)
E NEUROTROPHIC FACTOR/CT
L11 141 S E10
L12 2554 S E26
E E25+ALL
L13 789 S E3-E5 AND BRAIN DERIVED
L14 679 S E12,E13
L15 3242 S E2+NT (L) BRAIN DERIVED
L16 64 S L7 AND L8-L15
L17 19234 S INTERFERONALPHA OR ALPHainterferon OR INTERFERONBETA OR BETA1
E INTERFERON/CT
L18 302 S E3-E19
L19 18390 S E85-E101
E INTERFERONS/CT
E E3+ALL
L20 18391 S E7,E6 (L) (ALPHA OR BETA)
L21 546 S L7 AND L17-L20
L22 2340 S TIMP() (I OR 1)

FILE 'REGISTRY' ENTERED AT 15:29:36 ON 02 FEB 2004

L23 1 S 140208-24-8

FILE 'HCAPLUS' ENTERED AT 15:30:37 ON 02 FEB 2004

L24 2026 S L23
L25 859 S TISSUE INHIBITOR(1W)METALLOPROTEINASE 1
L26 27 S METALLOPROTEINASE INHIBITOR 1
L27 651 S TIMP1
L28 12 S FIBROBLAST COLLAGENASE INHIBITOR
L29 91 S L7 AND L22,L24-L28
L30 678 S L16,L21,L29
L31 9815 S IFNALPHA OR IFNBETA OR ALPHAIFN OR BETAIFN OR IFN(A) (ALPHA OR
L32 119 S L7 AND L31
L33 700 S L30,L32
L34 62 S L33 AND (FUSION OR FUSE OR FUSED OR FUSES OR FUSING)
L35 167 S L33 AND RECOMBIN?
L36 44 S L33 AND CHIMER?
L37 202 S L34-L36
E ROSEN C/AU
L38 27 S E3,E4
E ROSEN CRAIG/AU
L39 625 S E3-E5
E HASELTINE W/AU
L40 302 S E3,E4,E7-E10
L41 10 S L33 AND L38-L40
E HUMAN GENOME SCI/PA,CS
L42 975 S E5-E37
L43 13 S L33 AND L42
L44 13 S L41,L43
L45 13 S L44 AND L37
L46 9 S L45 AND (SHELF LIFE OR SHELF LIFE)
L47 4 S L45 NOT L46
SEL DN AN 1 4
L48 2 S L47 NOT E1-E6
L49 11 S L46,L48
SEL RN
DEL SEL
E FUSION PROTEIN/CT
L50 11933 S E9
E E9+ALL
L51 3795 S E3,E4

L52 5 S L51 AND L33
 L53 29 S L50 AND L33
 L54 34 S L49, L52, L53
 L55 27 S L54 AND ALBUMIN
 L56 7 S L54 NOT L55
 L57 159 S L37 AND ALBUMIN
 L58 132 S L57 NOT L43-L49, L52-L56
 L59 6 S L58 AND L16
 L60 7 S L58 AND L29
 L61 121 S L58 NOT L59, L60
 L62 96 S L61 AND (PD<=20000412 OR PRD<=20000412 OR AD<=20000412)
 SEL DN AN 9 12 13 24 29 31 35 39 44 47 55 58 72 74 83 85 92 93
 L63 18 S L62 AND E1-E54
 L64 29 S L49, L63 AND L1-L22, L24-L63
 L65 29 S L64 AND ?ALBUMIN?
 L66 29 S L64 AND (INF? OR INTERFERON OR TIMP? OR NEUROTROPHIC?)

FILE 'HCAPLUS' ENTERED AT 16:00:16 ON 02 FEB 2004

FILE 'WPIX' ENTERED AT 16:01:33 ON 02 FEB 2004

L67 9861 S L6/BIX
 L68 318 S L8/BIX OR L9/BIX OR L10/BIX
 L69 1564 S L17/BIX OR LL31/BIX
 L70 80 S L22/BIX OR L25/BIX OR L26/BIX OR L27/BIX OR L28/BIX
 L71 124 S L67 AND L68-L70
 L72 11209 S ?ALBUMEN?/BIX OR L67
 L73 513 S (A61K038-38 OR C07K014-76 OR C07K014-765 OR C12N015-14) /IC, IC
 L74 11377 S L72, L73
 L75 2983 S V275/M0, M1, M2, M3, M4, M5, M6 OR (B02-V03 OR C02-V03 OR B04-H05A
 L76 2604 S (A61K038-21 OR C07K014-52 OR C07K014-555 OR C07K014-56 OR C07
 L77 216 S L74 AND L75
 L78 111 S L74 AND L76
 L79 129 S L74 AND L68, L69, L70
 L80 311 S L77-L79
 L81 3 S L80 AND (ROSEN C? OR HASELTINE W?) /AU
 L82 7242 S (D05-H12B OR D05-H12B2) /MC
 L83 58614 S (B04-C01? OR C04-C01? OR B04-N02? OR C04-N02?) /MC
 L84 144 S L80 AND L82, L83
 L85 15 S C07K019/IC, ICM, ICS AND L84
 SEL DN AN 1 4 5 6 7 12
 L86 6 S E55-E66 AND L85
 L87 6 S L81, L86
 L88 6 S L87 AND L67-L87

FILE 'WPIX' ENTERED AT 16:25:05 ON 02 FEB 2004

FILE 'HCAPLUS' ENTERED AT 16:25:16 ON 02 FEB 2004

FILE 'REGISTRY' ENTERED AT 16:26:59 ON 02 FEB 2004

L89 1 S 507485-69-0
 L90 1 S 472960-22-8

=>